2009
Annual Report
TATRC

Telemedicine & Advanced Technology Research Center
United States Army Medical Research and Materiel Command

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"We must learn to share information and knowledge across boundaries and outside silos."

- Major General James K. Gilman
Commanding General, USAMRMC

"To improve the quality of our health care while lowering its cost, we will make the immediate investments necessary to ensure that, within five years, all of America's medical records are computerized."

- President Barack Obama

Contents

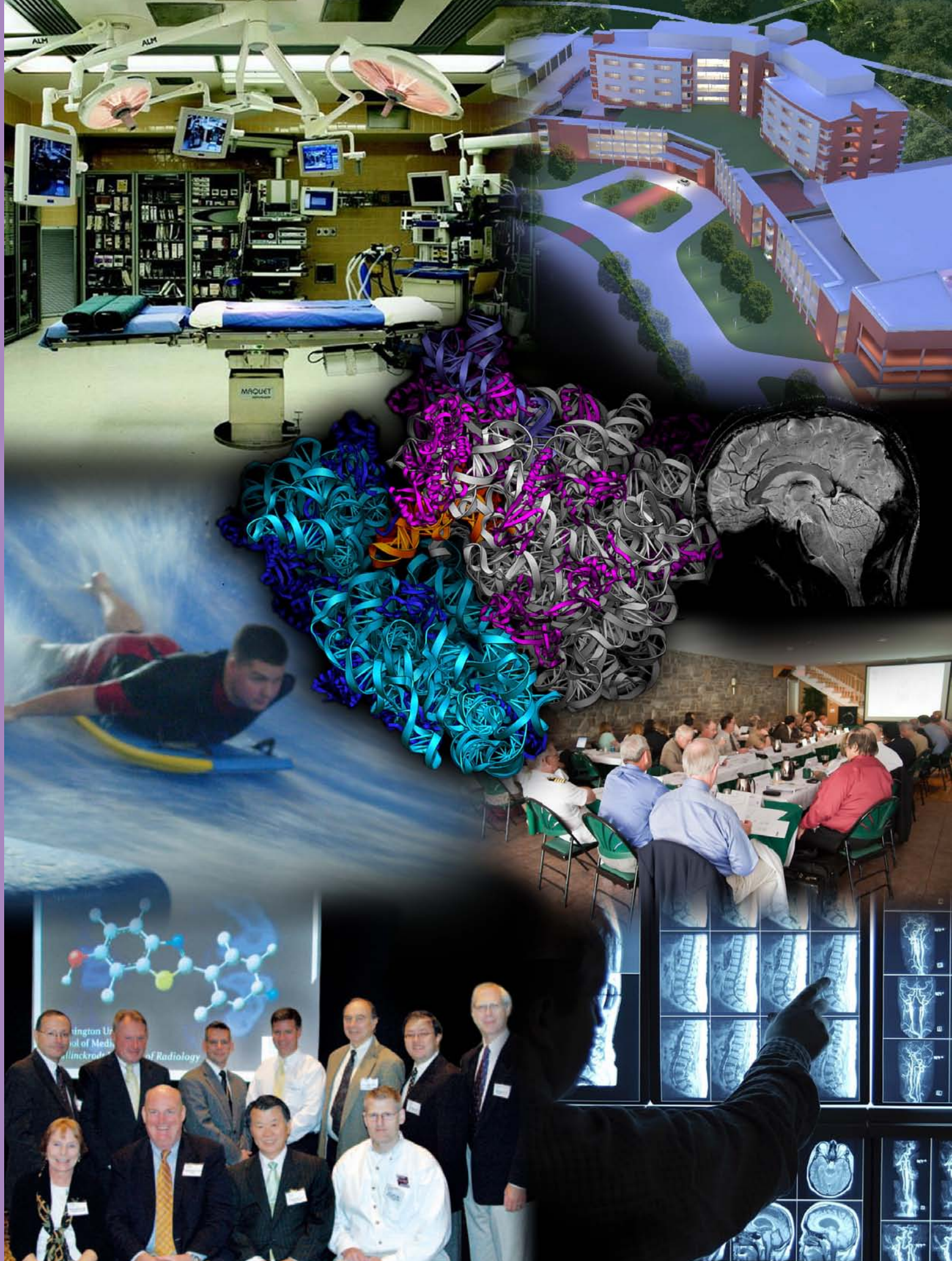
Introduction to TATRC

COL Fred Goeringer and MAJ Robert de Treville, in 1996, examine a surgical light in a mobile surgical center at Fort Detrick. A television camera could be mounted on the light and its signal beamed by a mobile satellite station to doctors hundreds or thousands of miles away.

The Telemedicine & Advanced Technology Research Center (TATRC) performs medical research reconnaissance and special operations to address critical gaps that are underrepresented in other Department of Defense (DoD) medical research programs. TATRC is an office of the headquarters of the US Army Medical Research and Materiel Command (USAMRMC). The Center conducts research in specific key capability areas including health informatics, telemedicine/m-Health, and computational biology. TATRC is also responsible for promoting and managing national and international extramural research in other key areas, notably medical training systems, medical robotics, human performance enhancement technologies, medicine in austere environments, brain and behavior neurosciences, and tissue engineering technologies. Through an extensive network of partners and consultants, TATRC explores management models for innovation and technology transfer, and supports core medical research program augmentation opportunities provided by special types of funding such as congressional special interest, Small Business Innovation Research (SBIR) Program, Joint Incentive Funds (JIF), and through leveraging other federal partner programs. The focus is generally at both ends of the research spectrum, from supporting high-risk innovative research to placing those innovations into the hands of the Warfighter (i.e., transition to military applications and institutionalization of research products and findings).

Reality 2009

LTC Sloane Guy in 2009 performed surgery in Iraq with a head-mounted camera and other cameras that could be maneuvered by remote medical consultants. This illustrated TATRC's ability to provide in-theater telementoring and consultation on difficult cases, made possible by the newly available dedicated medical bandwidth and advances in practical lighter weight, lower power, and affordable electronic systems.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Director's Message

"TATRC is the reconnaissance unit of military medical research, paving the way for new options to better protect and care for the Warfighter."

COL Karl Friedl
Director, TATRC

TATRC's philosophy includes the active shaping of science and engineering advances to address military medical needs. In 2009, TATRC stepped forward to organize and conduct, with our research partners, more important and militarily-relevant projects than ever before. TATRC's mission includes exploring science and engineering ahead of planned programs in the DoD, in order to create new options and embrace the advantages of new technology. TATRC also envisions moving laboratory findings to solutions for current military problems, and bridging the "valleys of death" in transition from discovery to solutions to implementation. Thus, TATRC functions like a macro-level ribosome, transforming the whole into more than the sum of its parts. This annual report highlights a year of achievements that benefited our Warfighters, and the many people who helped make them happen.

Discovery

Early in the year, Chuck Peterson, our chief scientist, pronounced this to be the year of the ribosome and, later in the year, the Nobel Prize in Chemistry went to three scientists who helped elucidate structure and function of the ribosome. Ribosomes are the central translational elements that produce proteins, and the next huge step on the path to understanding the biological networks underlying the human phenome, now that the human genome has been characterized. Understanding this translational apparatus also provides new targets for effective antibiotics, an understanding of cellular injury that underlies acute combat trauma as well as long latency neurodegenerative disease, and a new level of discovery amenable to the tools in this rapidly evolving era of information science. As an example, the TATRC-funded Greengard Laboratory at Rockefeller University has developed and employed a breakthrough technique, Translating Ribosome Affinity Purification (TRAP), to distinguish differential susceptibilities of neuronal cells based on their translational profiles. This opens the door to new targeted interventions for problems ranging from depression to Parkinson's Disease (PD) for Warfighters exposed to psychological trauma, head trauma, and potentially neurotoxic chemicals.

This year, Jaques Reifman's research team at the Bioanalysis Institute published numerous basic research papers on characterizing proteins and their complex behaviors and interactions (see pages 25-29). Their phenomenal record of research collaboration to bring new computational tools to bear on bioanalytics supports a range of solutions from rapid analysis of threat pathogens to physiological predictions. This work will help sustain the performance of Warfighters in the field and monitor the status of injured Warfighters during evacuation. Other major investments this year in systems biology include targeting traumatic brain injury (TBI) and models of PD, both of which hold promise for development of easily accessible blood biomarkers of region and cell-specific brain damage. More specific identification of injured brain areas, particularly once correlated with neuropsychological and clinical alterations, contribute to enhanced rehabilitation of our wounded Warriors.

Successes

In 2009, TATRC realized several key objectives and achieved the exit criteria to declare success. We declared success in our Hospital of the Future initiative led by Ms. Amy Nyswaner, supporting and influencing the Health Facility Planning Agency with new concepts in integrative health, healing environments, and new operating room design and technologies. The seeds sown in this effort such as patient safety, systems interoperability, and patient-specific surgical simulation and rehearsal will be incorporated into new hospitals being built, and picked up in other portfolios and through continued research in major programs, such as those at the Center for Advanced Surgical and Interventional Technology (CASIT), the Center for Integation of Medicine and Innovative Technology (CIMIT), and the University of Maryland.

Neurotrauma research substantially moved from TATRC into the Combat Casualty Care Research Program (CCCRP) Research Area Directorate (RAD) 2, with new core funding for a concerted program and with the transition of Dr. Ken Curley to the RAD2 program office. Dr. Curley continues to reach back to TATRC as a portfolio manager for special programs in neurotrauma (serious head injury and spinal cord injury), and for support in organization coordination of all TBI research activities in the DoD.

For the first time in over 50 years, rehabilitative medicine, notably the Military Amputee Research Program (MARP), received substantial intramural support and recognition in COL Jan Harris' new Clinical and Rehabilitative Medicine Research Program (RAD4), and TATRC moved to a supporting role with renewed focus on further future technology development. The Centers of Excellence at Walter Reed Army Medical Center (WRAMC) also matured to a point where they will transition to core funding in the RAD4 program and move out of the TATRC nest. A key accomplishment of these centers has been the establishment of a personalized medicine model, focused on genomics-based diagnosis and treatment of cancers in women (pp. 85-90).

New Initiatives

This year, TATRC began planning for a new effort led by the Joint Technical Coordinating Group 1 (JTCG1, "Medical Training Systems and Health Information Technologies"). This is a tri-service research program that expands on two TATRC core competencies, with a first-time funding provision in the President's budget for a focused and sustained research and development program. The military medical community now has the opportunity to advance its specific research needs to put medical training systems on a par with aviation simulation and training and use advanced distributed learning models already developed in the DoD. We also have the opportunity to support the development of an electronic health records system with the Department of Veterans Affairs (VA) that will allow the best in patient care, with capabilities ranging from automated battlefield data capture, to genomics data for personalized healthcare, to "mineable" outcomes data to improve care and reduce costs. The current efforts in pharmacovigilance (pp. 140-141) provide one example of this approach. As the year ends, an announcement for advanced development of medical training systems ($40M) is being advertised to potential performers, and a similar announcement for health information technology is being finalized.

Several new initiatives were started or significantly advanced in 2009, notably a competitive research program for vision loss associated with combat-related head injury (pp. 118-123), a program to create a virtual human advisor (SimCoach) in direct support of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) (pp. 143-144), a demonstration project led by LCDR Steve Steffensen in direct support of the DoD-VA Interagency Virtual Lifetime Electronic Record (VLER) program (pp. 30-39), a new acoustic trauma portfolio built around new technology opportunities to advance hearing protection and restoration, and the m-Health initiative to use readily available mobile platforms such as the cell phone to deliver health care information and interventions to Warfighters in remote locations and to support Stability Operations in Combatant Command (COCOM)-led international health programs (pp. 45-50).

TATRC is an integral partner in the Joint Medical Distance Support and Evacuation (JMDSE) Joint Capability Technology Demonstration (JCTD) project for enhanced capabilities to augment and extend in-place combat casualty care (pp. 20-24). Extensive planning was completed this year for operational tests to begin in 2010. This effort, led by Dr. Gary Gilbert, provides a test venue for a variety of robotic, informatic, and biomonitoring technologies that have been developed over the past few years, as well as testing a controversial experimental concept of casualty evacuation by unmanned aviation vehicles (UAV).

Future

Many other important efforts remain to be tapped. In 2010, TATRC will be looking for game changing or "disruptive" science and engineering breakthroughs in neuroimaging technologies, brown fat regulation of metabolism, radioprotection mechanisms and interventions, Vitamin D roles in Warfighter physiological resilience, neural training and neurobiological alterations and brain health, olfactory signals affecting emotion and learning, semantic organization of information and data, virtual environments for safe and effective training, novel indicators of wellness and functioning, and radical new medical applications for mobile communications devices. These represent examples of interventions, models, and tools that may potentially solve problems of high or unique prevalence for the DoD.

One of our grand challenges at TATRC is to develop the roadmaps for a "holographic doctor" when a human attendant is not available, and for just-in-time training and guidance to a human when a physician is not available.

In addition to our traditional quest to strengthen DoD partnerships with industry and academia, we expect to increase research effectiveness through expanded partnerships with other federal agency partners such as the VA (e.g., Northern California Institute for Research and Education (NCIRE) and San Francisco VA Medical Center (SFVAMC) (pp. 110-112), the Food and Drug Administration (FDA), NASA, and the Department of Health and Human Services (HHS), notably the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Center for Complimentary and Alternative Medicine (NCCAM) and the National Institute of Neurological Disorders and Stroke (NINDS). We will continue to improve research communication and coordination through TATRC convening functions such as the Product Line Reviews (PLRs) (pp. 159-168) and seek other novel exchanges to facilitate transition of discoveries to solutions to implementation. We will also be looking for opportunities to advance military to military exchanges in medical research with some of our international partners, notably France, Germany, the United Kingdom, and Norway, and medical-scientific exchanges with other countries. Every new year seems even more promising and exciting than the year before, but for TATRC accomplishments, 2009 will be tough to top.

TATRC Investment

FY06-09 Investment

Since 2006, TATRC has been responsible for over $1.3B in research funding, representing four cycles of annual appropriations (FY06-FY09). Half of the distinct congressional special interest line items over these four years have been represented in a half dozen key topic areas, with trauma/surgical care and health information technologies topping the list.

FUNDING FAST FACTS FY09

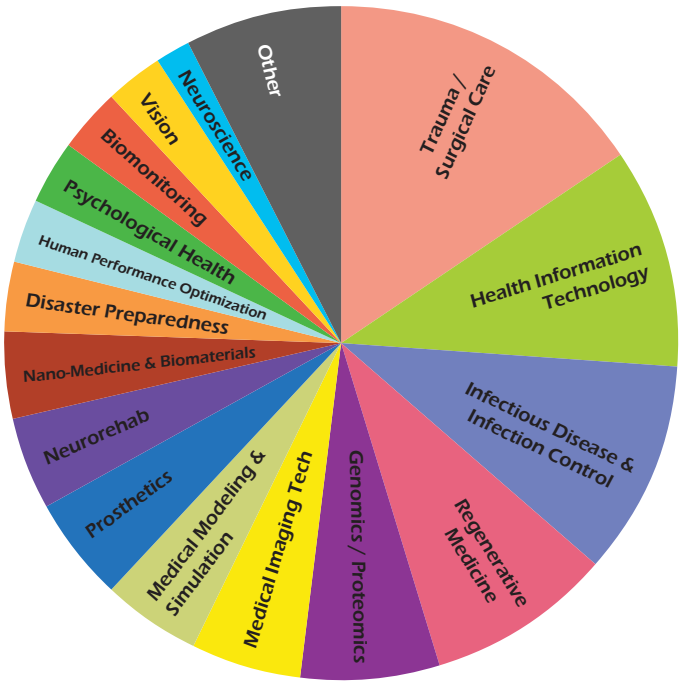
- $423M Congressional Special Interest (165 individual projects)
- $22.4M SBIR/STTR
- $4.8M AAMTI
- $1.4M Operational Telemedicine
- $31.4M Other Funding (including P8 m-Health initiatives)

Projects are geographically distributed across the US, and include efforts in other countries, but areas of special concentration include Boston, MA, Hawaii, California, Pittsburgh, PA, Houston, TX, and Nebraska.

The distribution of congressional special interest projects over the past four years is shown in the pie charts, with a breakout of individual line items and of dollars invested in the major TATRC portfolio areas. Six areas predominate in these categorizations, but regenerative medicine and biomonitoring technologies together lead the way for intellectual property (patents filed).

TATRC has a zero net cost to the Army or the DoD, operating from management costs directly tied to the managed funds. Services are provided to ensure that research is connected to military interests (in addition to satisfying Congressional intent)

FY06 - FY09
Total Number of Separate Projects by Topic Area
(many recur through each year but are counted only once)



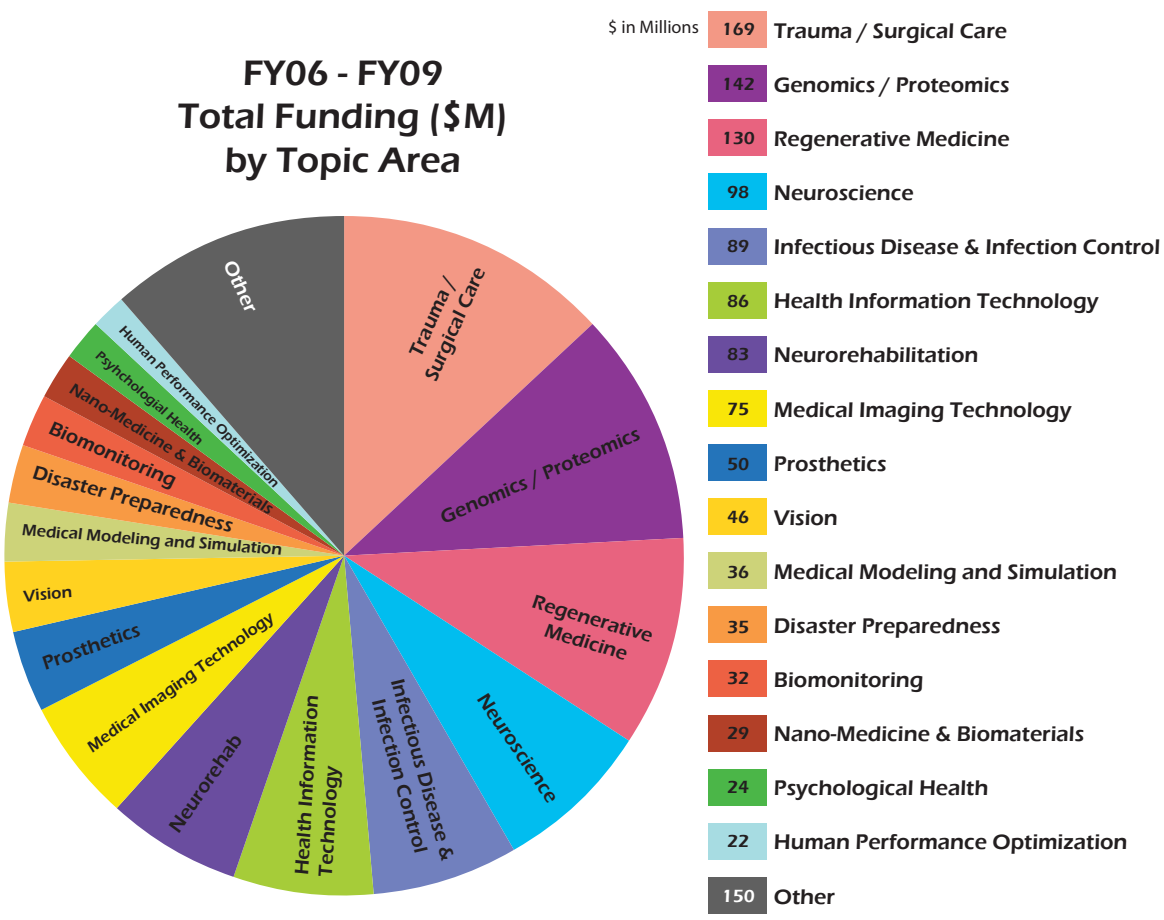
54	Trauma / Surgical Care
37	Health Information Technology
37	Infectious Disease & Infection Control
31	Regenerative Medicine
23	Genomics / Proteomics
19	Medical Imaging Technology
17	Medical Modeling and Simulation
17	Prosthetics
16	Neurorehabilitation
14	Nano-Medicine & Biomaterials
12	Disaster Preparedness
11	Human Performance Optimization
11	Psychological Health
10	Biomonitoring
10	Vision
6	Neuroscience
27	Other

such as convening functions, research collaborations and augmentation, and transition to application and/or commercialization.

The return on investment from various projects within the TATRC portfolio has been sizeable. Outcomes range from new investigators trained and mentored to major new programs established and spun off into other programs or implemented by the military. More frequently now, new planning considers criteria for an "exit strategy," so that TATRC can declare success with a problem and move to new challenges instead of slicing the resource pie ever thinner. A phenomenal medical research base/capability has been created for the DoD and is producing ever greater responsiveness to new problems and challenges. This is reflected in current efforts and new TATRC initiatives. TATRC constantly reevaluates strategic and technical azimuths for the smart investment of taxpayer dollars.

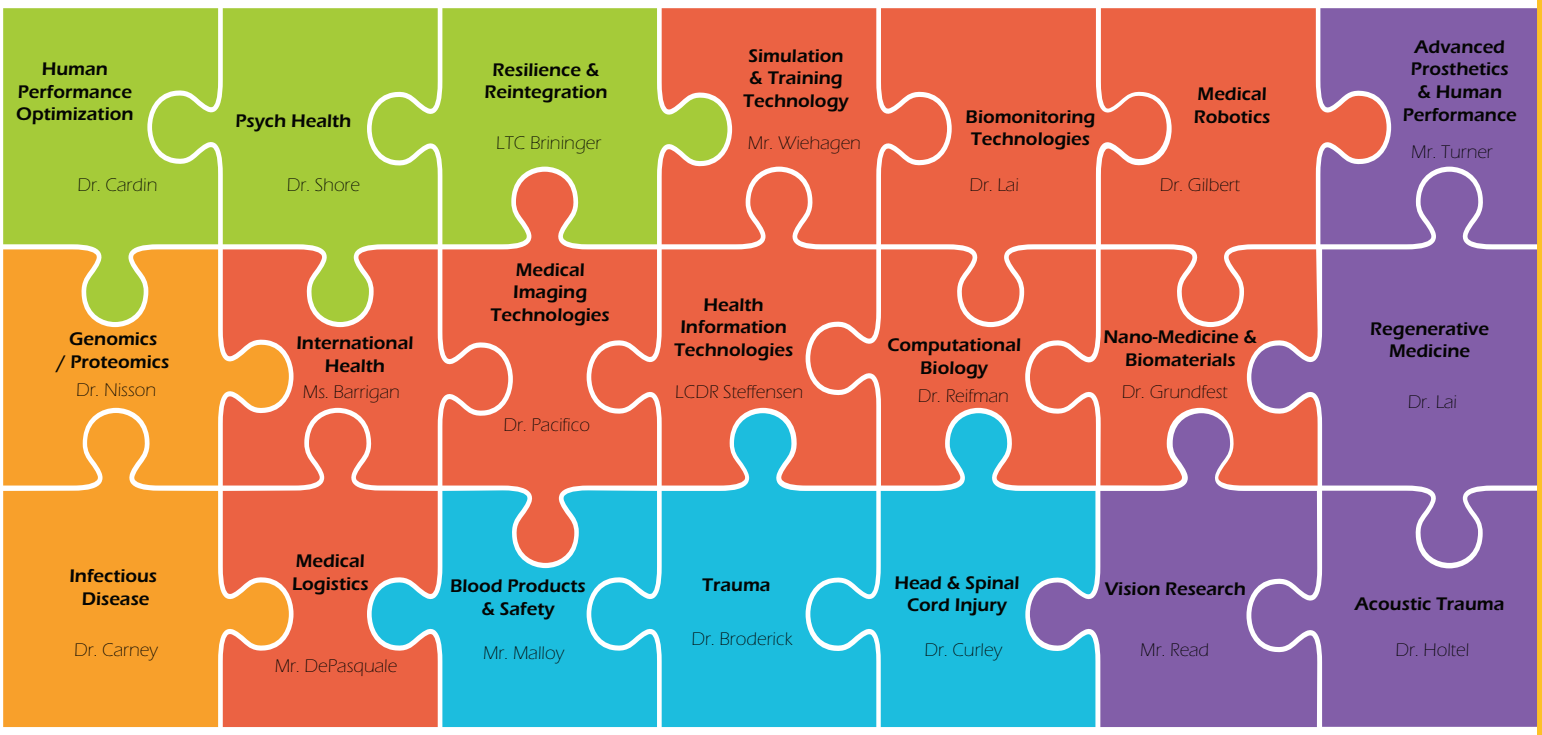
In a series of workshops, TATRC and partners expanded on several strategic objectives. Three workshop themes were chosen as exemplars of TATRC programs: Hospital of the Future, Medical Simulation, and Pain Management. Some common priorities came out of each workshop, as well as specific objectives that will be addressed in related portfolios such as modeling and simulation:

- Interoperability, simulation training, communication/distance medicine;
- Develop requirements documents, advance simulation curriculum development, investigate new technologies, and evaluate role and direction for cognitive simulations;
- Develop comprehensive approaches to pain that aid the Warfighter from an acute situation to the chronic alleviation of pain syndromes.



Portfolios

The figure below outlines the current portfolios and strategic initiatives at TATRC. Each portfolio is responsible for oversight and management of a number of projects in the respective areas of interest. The type of science nurtured by TATRC inherently transcends scientific and disciplinary boundaries. Thus, it is important that there is constant communication through all parts of the puzzle to create the current whole. It is also axiomatic that the areas of interest and priority will change. Such changes are reflected by addition and subtraction of current identified portfolios and priorities. TATRC takes pride in being current, flexible, and communicative throughout a highly diverse organization. The "portfolio puzzle" below reflects this continuing quest to "put the pieces together."



Relationship to DoD Medical Research Joint Technical Coordination Groups (JTCG)

- JTCG-1 Medical Training Systems & Health Information Technologies
- JTCG-2 Infectious Diseases
- JTCG-5 Military Operational Medicine
- JTCG-6 Combat Casualty Care
- JTCG-8 Clinical & Rehabilitative Medicine

Simulation & Training Technology

Simulation & Training Technology

The Medical Simulation and Training Technology Portfolio began in 1999, with a vision to improve medical training from the foxhole to the operating room, and beyond. After a decade of investment, and based on years of input from many sources, the vision has broadened. TATRC now seeks to facilitate a paradigm shift in medical training, from a subjective mode of skills assessment to a curriculum-aligned, metrics-driven, objective system to assess proficiency of skills.

Based on a strategic plan developed on input from a 70-person Integrated Research Team in 2000, and re-confirmed by a 50-person Integrated Product Team meeting in 2008, TATRC is funding and managing research in four broad categories: PC-based interactive multimedia; digitally enhanced mannequins; part-task trainers; and total immersion virtual reality. The technical strategy is to identify and develop "enabling technologies" into components that can be integrated into systems of simulation-based training, then assess them to determine the degree to which they transfer skills learned via simulation to the delivery of care. Examples of enabling technologies include real-time *in vivo* tissue property measurement, haptics, tool-tissue interactions, graphics and visualization, learning systems, and metrics development. A number of examples follow.

Autonomous Casualty Simulator

The Combat Medic Training System (COMETS) project by the CIMIT SimGroup is developing a prototype autonomous casualty simulator for combat medic trauma training. COMETS is a physiologically based, self-contained autonomous system that will respond to treatment as a human casualty would. Actions performed on it will be reported as after action reports automatically, without instructor input. By design, multiple COMETS units can be used in a mass casualty exercise with only a single instructor observing treatments. The COMETS project began several years ago, based on input from a multi-specialty team with Army Medical Department (AMEDD) combat medic advisors as Subject Matter Experts.

Winter Institute for Simulation Education Research (WISER)

The Winter Institute for Simulation Education Research (WISER) began a training effectiveness study in October 2009, which examines the degree to which

The Medical Simulation and Training Technology Portfolio's vision to improve medical training has broadened. It now envisions the use of a curriculum-aligned, metrics-driven system to assess skills proficiency, rather than the conventional subjective assessment method.

Portfolio Team

Gene Wiehagen
MAJ Brett Talbot
Harvey Magee
Dr. Kevin Kunkler
Jason Ghannadian
Greg Wimsatt

mannequin-based training affects demonstrated proficiency to respond to airway management, hemorrhage control, and tension pneumothorax.

Departments of Combat Medical Training – Technology Enhancement

BearingPoint, Inc. (now Deloitte Consulting LLP). seeks to reduce the number of persons needed to conduct the All Skills Practical Exam and reduce the amount of time the candidates must wait to receive the results of their skills evaluation. This is a significant challenge to both military and civilian training departments. BearingPoint (Deloitte) has completed research, design, and development of a technical solution: to digitize and integrate forms-based testing and training documents into the 68W training program to improve the quality of combat medic training. This includes the digital conversion of paper to electronic forms, processing of radio frequency identification (RFID) signals using passive tag technology, two-way secure wireless synchronization of the tablet, and central servers managing the data.

Medics and trainers utilize advanced technologies to streamline training and evaluation techniques.

Blended Learning Ecologies (BLE) in the Military: Comparative Studies for Combat Lifesavers and their Instructors

The University of Nevada Las Vegas is researching Blended Learning Ecology (BLE), a model that strategically integrates fact to face instruction with technology mediated instruction. Several studies, using both quantitative and qualitative methodologies, will assess how effective the BLE model is compared to traditional Classroom Based Instruction (CBI) in the training of Warfighters and their instructors. This project is performed in coordination with the Pennsylvania National Guard in support of Combat Lifesaver (CLS) training, and to assist with CLS conducted at both the basic training locations and refresher training at National Guard sites.

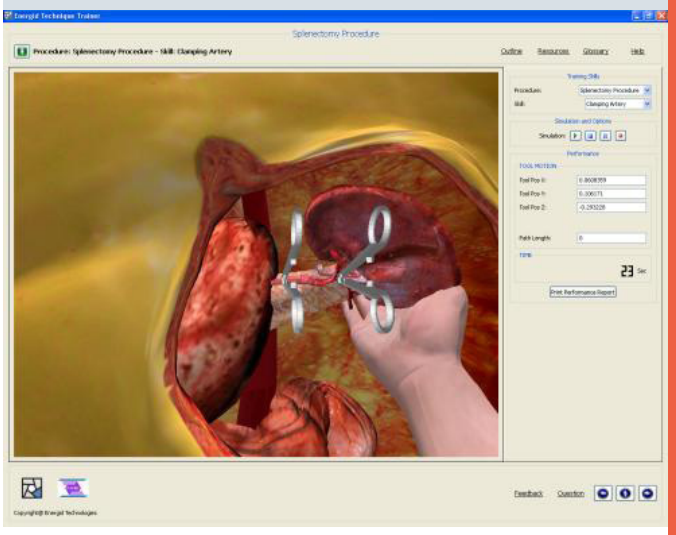
Haptics-Optional Surgical Training System (HOSTS) – SBIR Phase II

Haptics-Optional Surgical Training System (HOSTS) is developing an innovative surgical training system that will allow trainees to effectively learn a surgical technique and be able to repeatedly rehearse parts of or the entire procedure. Energid Technologies developed a PC-based simulator to train for a splenectomy procedure.

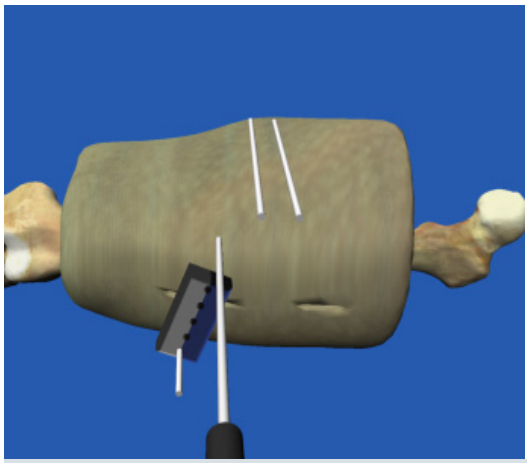
Simulation-Based Open Surgery Training System (SOSTS)

A personal computer-based Simulation of Open Surgery Training System (SOSTS) is a developmental platform to obtain surgical metrics (of devices, instruments, and their use in procedures of surgical technique), and to develop and evaluate new open surgical procedures and advanced medical devices. The goal is to improve training so surgeons can

Screenshot from PC-based splenectomy trainer being developed by Energid Technologies.



obtain and maintain proficiency in the performance of open surgical procedures. TATRC envisions an open architecture surgical simulation platform that allows the rendering and use of virtual versions of actual instruments used in trauma surgery. A final goal is to enable novel surgical instruments to be "scanned" and "virtualized" or entered into the simulator before they reach physical prototype stage and then evaluated. The SOSTS has potential to reduce surgical errors, improve patient safety, reduce cost, improve access to care in fixed medical treatment facilities, and improve medical educational training programs. This technology will also allow the assessment of novel surgical instruments and techniques "in silico" in turn limiting use of animals and reducing development costs. Two examples are listed below.



The fractured femur simulation will cause the trainee to consider a full spectrum of situations both operative and non-operative.

Fractured Femur Simulator

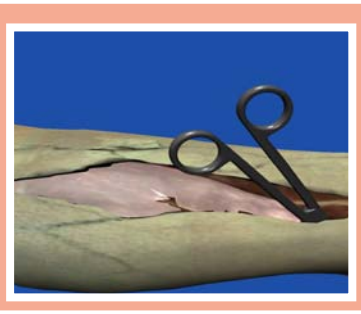
The objective of this SBIR project is to develop a realistic simulation for the treatment of a fractured femur. The simulation will train the trainee to consider a full spectrum of situations including major arteries, veins, and nerves, patient age, splinting and traction, operative and non-operative treatments, pain management, and rehabilitation. Two companies, Simulution, Burnsville, MN and Touch of Life Technologies, Aurora, CO, are concluding their studies and will follow-up with formal training effectiveness studies.

Compartment Syndrome Simulation System

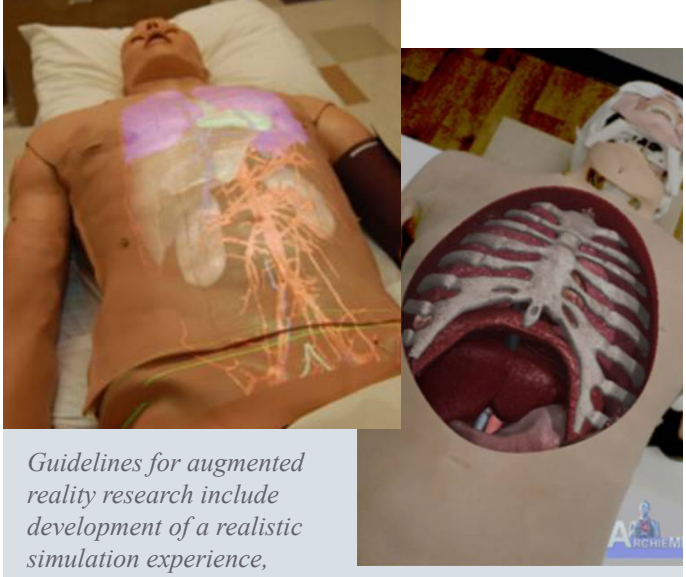
Touch of Life Technologies, has been selected to conduct advanced work under the SBIR Commercialization Pilot Program. The objective is to produce a highly adaptable virtual environment for training diagnosis and treatment of compartment syndrome, which will result in a production prototype of the system. It will include an easily adaptable virtual reality (VR)-based simulator in which to practice diagnosis and treatment (including fasciotomy) of compartment syndrome of multiple extremities including the leg.

Augmented Reality for Medical Applications

QinetiQ (Farnborough, England) is developing technology to demonstrate that the registration of synthetic imagery with a live patient is possible. This will essentially provide projected maps over a patient to guide a surgeon to specific imaged targets. QinetiQ is using a combination of sensors, computer vision and materials engineering.



Simulation and Training Technology examples include the Wintab touch screen integration (left), which demonstrates the abdomen cutting and clamping of an artery during a simulated splenectomy procedure. and the Compartment Syndrome simulator (right), which will be part of an extremities trauma simulator and will be displayed on a Common Platform Simulator that can deliver training for other surgical skills, as well as extremities trauma.



Guidelines for augmented reality research include development of a realistic simulation experience, proper rendering and sizing of visual images, interaction between trainee and "patient," ability to convert MRI images into functional visual formats quickly, monitor patient's vitals, and embedding of metrics to assess trainee performance. Photo courtesy ArchieMD.

Data Driven Optimization of Surgeon Skills for Enhanced Training, Simulations and Assessment

The William Beaumont Hospital, Royal Oak, MI, is working to optimize surgical skills to enhance training and assessment. Using their surgical test bed for physically based robotic and laparoscopic simulations, researchers are adding motion tracking and sensor data capture and an augmented reality system to model new and challenging scenarios. Built-in sensing systems provide error-tracking capabilities for trainee feedback; and automatic data collection methods will be used to define task-specific metrics for each component of a surgical skills task set lists. A unique component is the creation of augmented reality by adding to the simulated surgical environment with virtual objects added graphically to the live video. Expert surgeons will provide baseline data on specialty-specific tasks. This will allow assessment of the skill levels of the existing surgical pool and benchmark parameters for training of novice surgeons. Some US Army surgeons will participate in the study. A reset training protocol will be designed that could be used by surgeons in pre-deployment training and by surgeons returning from deployment to identify and remediate skills that have deteriorated after prolonged absence from specialty-specific experience.

Medical Simulation Training for First Response to Chemical, Biological, Radiological, Nuclear or High Explosive Events (CBRNE) – SBIR

The focus of this research is the development of a training system that supports participation in, and response to, chemical, biological, radiological, nuclear, and high yield explosives chemical, biological, radiological, nuclear, and high yield explosives (CBRNE) events. Forterra Systems has been selected for a Commercialization Pilot Program (CPP) using a multi-player sim-game approach for team training. Combining medical simulation with virtual world technology focused on simulating human interaction creates numerous opportunities for building medical training applications focused on diagnostic, treatment, situational awareness, and teamwork skills. With this approach it is possible for individuals to receive group training without leaving the comfort of their home or office.

Pandemic Influenza

This research area focuses on preparing healthcare providers to respond to an infectious disease outbreak such as a pandemic influenza or tropical disease. Users will be able to perform mul-

Interface for remote access to simulations. (image provided by SimQuest LLC)

tiple tasks and strategies for control of an outbreak. A scenario editor allows variables to be changed such as patient numbers, arrival patterns, equipment availability, staffing patterns and availability, etc. Two companies (SimQuest LLC, Silver Spring, MD and Total Immersion Software, Inc. Hampton, VA) are currently engaged in SBIR Phase II research.

Ultra-High Resolution Display for Army Medicine (UHRDARM)

The purpose is to develop an ultra-high resolution (greater than High Definition), wide field of view, head-mounted display that is powerful, lightweight, and applicable both to medicine and other fields as well. This display accepts input from any PC/ Macintosh source. Based on congressional funding, eMagin, Hopewell Junction, NY, is actively engaged in its third year of research.

The Ultra-High Resolution head-mounted display is being developed by eMagin.

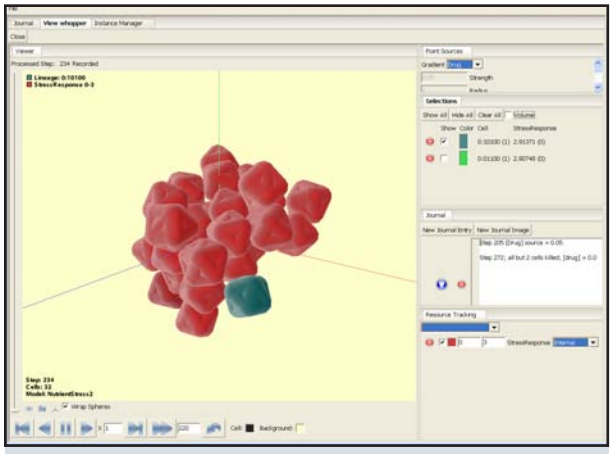
High Fidelity Computer Modeling of Epithelial Tissue

Crowley-Davis Research, Inc., Eagle, ID, builds upon the development of enabling technology incorporating biologically derived principles in rule-based encoding systems, based on high-fidelity computer modeling of epithelial tissue development. Research is progressing to create a patch of interfollicular virtual human epidermis with a dynamic and diverse range of physiological response to chemical agents, bacterial toxins, and viral infection. This project will also generate simulations suitable for studying and teaching mechanisms of epithelial development and

organization, and will develop multi-purpose simulation technologies for making the modeling platform Internet-accessible by independent researchers and educators.

University of Maryland Medical Center Laparoscopic Ventral Hernia Procedure

A model has been developed that portrays realistically the laparoscopic hernia repair within a Stryker physical trainer box. Trainees are challenged via simulation to remove adhesions, measure the size of the hernia, prepare an appropriately sized meshed cover, insert and staple the mesh to affect a hernia repair.



Screenshot, courtesy of Crowley-Davis Research, Inc. of a program being developed to predict human epithelial cell growth with response to various conditions including biochemical agents.

Medical Training Systems in Development

Trainer	Research Organization	Summary
	PC-Based Interactive Multimedia	
OLIVE	Forterra Systems	Developed a virtual world program (OLIVE) that can be used to train individuals in advanced distributed group training scenarios such as CBRNE training.
Virtual Human Patient Trainer	University of Southern California Institute for Creative Technologies	Developed a Virtual Human Coach for individual confidential Soldier interaction over the internet for "face-to-face" behavioral health questions and issues. This coach will remember interactions with individuals, and provide a safe sounding board and portal to medical resources.
IED Simulator	MYMIC LLC	Developing a Complex Incident Response Training System-Combat Medic (CIRTS) that will allow medics to train for casualty and site management using a matrix style progressional learning progression.
	SimQuest International	Developing a simulation-based game to train prehospital care providers in decision-making processes for effective scene and patient management after an IED.
Rapid Trauma	SimQuest International	Developing a software-based program to train predeployment trauma surgeon skills, with focus on decision-making skills for combat trauma cases and scenarios, and review of surgical approaches not seen in peacetime practices.
	Digitally Enhanced Manikins	
Combat Medic Training System (COMETS)	Massachusetts General Hospital Corporation	Developed a completely autonomous highly realistic prototype casualty simulator that is able to withstand harsh field conditions and decontamination during combat trauma and chemical, biological, radiation, nuclear, explosive (CBRNE) exercises; emphasis on durability, ease-of-use, and cost-effectiveness for the next generation of casualty simulators.
	Part-task Trainers	
Virgil Chest Tube Insertion Simulator	Center for Integration of Medicine & Innovative Technology	Developed the Virgil Chest Tube Insertion Simulator, a chest trauma training system for combat medics, using realistic anatomy in a visually advanced training curriculum.
Compartment Syndrome Simulator	Touch of Life Technologies	Developed a virtual training platform for compartment syndrome with haptic feedback and adaptable for multiple uses.
Rapid Trauma Skills Trainer	Operative Experience, Inc.	Developing a realistic simulation-based course for open trauma surgery at lower cost and greater availability than animals or cadavers, using a goal-directed curriculum, instructional videos, operations on artificial body parts, and objective metrics for evaluation.
Ophthalmology Surgical Simulator	Touch of Life Technologies	Developed a simulator to practice globe repair, most steps of phacoemulsification, and ultrasound for diagnosis and measurement; will be coupled with a mentor program, which combines HTML, interactive anatomic animations, and direct proficiency measures from the simulator.
Burr Hole Simulator	SimQuest International	Developed a virtual workbench, part-task simulator for training medical personnel to perform emergency neurosurgical procedures including opening depressed skull fractures and removing bony fragments; drilling a burr hole into the skull; and elevation of a bone flap for bleeding control.
Cricothyrotomy Simulator	National Capital Area Medical Simulation Center	Developed a simulator in which the user can perform a cricothyrotomy on a virtual patient in 3D with haptic feedback.
	Total Immersion Virtual Reality	
CAREN	Center for the Intrepid and Military Advanced Training Center	Enhanced applications of a Computer Assisted Rehabilitation Environment (CAREN), a virtual reality environment in which the agility of healthy subjects and rehabilitation patients can be tested and trained in a variety of reproducible conditions with near realtime feedback to the individual.

Biomonitoring Technologies

Biomonitoring Technologies

This portfolio addresses the challenges of monitoring the Warfighter's health/medical status from training and operation to medical evacuation and rehabilitation. Monitoring of the Warfighter's health also extends from the Warfighter's body to their environment to assess chemical and/or biological threats in the air or in the water. The information collected through these monitoring devices will improve Warfighter training and safety; provide medical situational awareness through analyses on current medical data of individual Warfighters and; evaluate rehabilitative therapies effectiveness. Further analyses of the collected data can be applied or used in medical modeling to assess and/or predict health and/or medical outcomes.

Areas of technological opportunities to affect a Warfighter's health and medical outcomes include development of devices applicable from training to rehab such as: wireless vital signs monitors, miniature medical sensors, and personal area networks. These technological advances allow for remote physiological monitoring of the Warfighter's health and enable continuous assessment of force health. In addition, the portfolio funds projects targeting specific and unaddressed military medical needs. These include early detection of kidney injury and quantification of blood propofol levels. Some project examples meeting these technological advances and targeted military medical needs are highlighted here.

Wireless Vital Signs Monitor on a Band-Aid for Combat Casualty Triage and Medical Evacuation

L-3 Services is developing a novel, wireless vital signs monitor for effective combat casualty triage, medical evacuation, and patient tracking on a band-aid like configuration. The proposed platform will be a single use, sensor-on-a-strip (SOS) with geographic information system (GIS) to track movement of patients. The band-aid like device will provide important vital signs such as heart rate, blood pressure, and oxygen saturation to monitor casualties across echelons from point of injury and throughout a patient's transport. Some advantages to this approach include small medical footprint (size and weight), patient identifier, patient tracking, low cost, and single-use (i.e., contamination free).

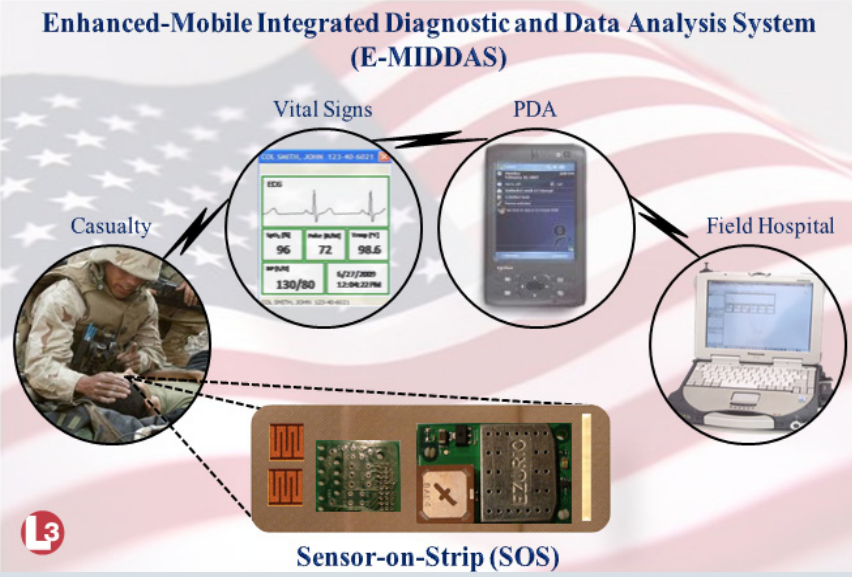


Illustration of E-MIDDAS Sensor-on-Strip (SOS) design and the information it collects and transmits.

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TATRC is actively supporting its research partner, L-3 Services, to ensure the development of this technology platform will meet the needs of the combat medics and meet the requirements for field deployment by facilitating meetings with combat medics and developers. Taking a longer look at the possibility of expanding the device's utility and lifecycle, TATRC also facilitated an L-3 Services meeting with medical modelers at the US Army Institute of Surgical Research (USAISR), to learn the vital signs data currently being evaluated for input into the algorithms for shock detection. Since data collected from the device can be wirelessly transmitted to the combat medic wrist unit (which will be designed to monitor up to several casualties at a time), data can be either wirelessly transmitted from the device or the wrist unit to a central server and feed various medical algorithms that are used to assess and/or predict patient's health outcome. Finally, TATRC continues to look for innovative sensor designs for integrating onto this SOS to further reduce the medical footprint and power need.

Schematic illustration of the University of Connecticut implantable biosensor for metabolic monitoring consists of a remote telemetry such as a watch, that operates the implantable biosensor.

Wireless, Miniature Medical Sensors

TATRC continues to find and fund cutting edge medical sensor development that enables remote, wireless, and continuous monitoring of Warfighter's medical and/or health status. Such innovation can provide a technological advantage in managing the force health between physical or medical exams. TATRC takes calculated risks in funding identified technological gap/advantages to augment its research portfolio and the Army medical portfolio. Thorough reviews of current technologies and Army investments/programs, an independent peer-review system to assess proposal scientific merits assures risk mitigation along with continuous project monitoring. One such program is at the University of Connecticut at Storrs. A multi-disciplinary team of leading scientists including Drs. Diane Burgess, Faquir Jain, and Fotios Papadimitrakopoulos is developing the next generation of sensors that will enable remote, wireless, and continuous monitoring of Warfighter's physiological and medical conditions. This miniaturized, implantable biomedical sensor will provide for remote health and/or medical situational awareness of a Warfighter and is small enough to be inserted and removed via a 16-gauge needle.

To meet military medical needs, the team has designed a sensor to detect multiple analytes such as glucose, lactose, and oxygen. This minimally invasive biosensor has been designed with an outer hydrogel coating to release inflammation-suppressing agents, which could minimize the negative tissue response to the implant. The implantable functionality, which is targeted to have a lifecycle between one to nine months, will not interfere with the Warfighter's mission or require the Warfighter to don the device.

Since TATRC's initial seed funding, this biosensor has garnered additional grant support, which will allow the team to initiate and meet the next challenge identified by an independent, scientific and military panel in 2008: to start the integration design into a single implantable device (i.e., integrating multiple components to include electrochemical sensors, wireless communication unit, programmable potentiostat, and signal processor).

Personal Area Network for Remote Physiological Monitoring

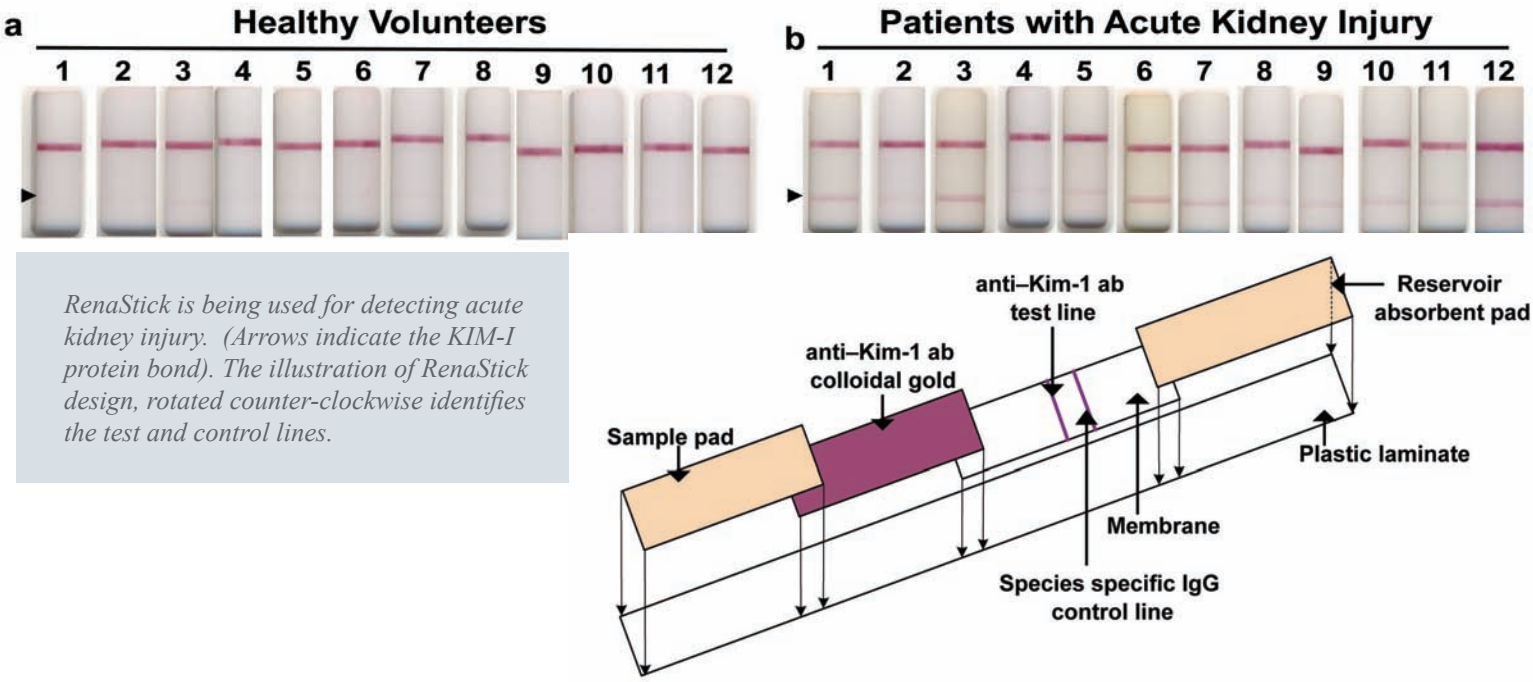
TATRC continues to partner with the US Army Research Institute of Environmental Medicine (USARIEM) to support the development of a personal area network for remote physiological monitoring. To meet this program objective, Elintrix has been contracted to develop an integrated system that will capture, analyze, communicate, display, and archive geo-location and physiologic-sensor data. The program consists of two projects to include Warfighter-worn elements of the Spartan network (SPARNET), which includes a squad-area-network (SAN) radio for Warfighter-to-Warfighter

A hydration unit with integrated SPARNET radio/processing unit and USARIEM fluid intake monitor. SPARNET is a body-worn, software-defined-radio and physiologic-algorithm processing unit that integrates a BIONET inductive link to sensors, which report via a three-axis accelerometer and inclinometer, GPS receiver, and contains a battery-charge monitor.

data communication, and a Personal Area Network (aka BIONET) radio for on-body communication. The BIONET radio is a modifiable, integrated, inductively-linked, minimalist, modular design with processing capability for use with sensor systems like the Warfighter Physiological Status Monitor (WPSM). BIONET supports transmission of data via a modulated magnetic field. Detection of the resulting short-range, bidirectional communications by hostile forces is made problematic due to the frequency and rapid attenuation of the magnetic field. SPARNET enables continuous monitoring of a Warfighter's geo-location and health status in the field to improve force health protection.

Early Detection of Kidney Injury

Acute renal injury, which can be fatal, can occur due to crush injuries, severe burns, and exposure to toxic chemicals. The current method for detecting acute kidney injury (AKI) is based on decades-old science to detect molecules in the blood that accumulate after kidney cells have died. This method fails to inform care providers to take countermeasures before serious damage occurs. Since combat wounds could lead to acute renal injury, TATRC decided to fund a novel technology to address this technological gap. RenaStick, developed by nephrologist Dr. Joseph Bonventre and toxicologist Dr. Vishal Vaidya at CIMIT, will enable medical personnel to take actions early on including aggressive countermeasures to prevent or treat AKI. RenaStick is designed to detect a protein, discovered and named by the researchers as kidney injury molecule-1 (KIM-1). Since KIM-1 is present in the urine within 3 to 6 hours following trauma and correlates with progression of AKI, the new method offers advantages in providing more time for physicians to address the medical situation, and increased sensitivity (KIM-1 increases more than a hundredfold and appears only when kidney is injured). The current method takes 12 to 14 hours for detection in the blood following the onset of kidney injury. The new method involves adding only a drop of urine sample to gold nanoparticles coated with KIM-1 antibodies and placing this on a small strip of paper. KIM-1 molecules present in the urine attach to the antibodies and are absorbed up into the paper. A different antibody on the strip of paper stops the KIM-1 absorption process and a resulting red line appears. The darker the shade is the more KIM-1 molecules are present in the urine and indicates the severity of the injury. In addition, a portable machine reader has been designed to quantify the level of KIM-1 present. Also, the FDA and its equivalent in Europe are encouraging the use of KIM-1 detection in drug development to ensure kidney safety. The team plans to market RenaStick within the next year.



RenaStick is being used for detecting acute kidney injury. (Arrows indicate the KIM-I protein bond). The illustration of RenaStick design, rotated counter-clockwise identifies the test and control lines.

Target: Infusion for Anesthesia, Quantification of Blood Propofol Levels

Developing a simple, safe, and reliable method to quantify the real time Propofol levels in blood serum of patients during surgery is important, since currently there is no way to quantify the drug levels in patients. In addition, TATRC has identified automated drug delivery systems for use during MEDEVAC that would address a technical gap and reduce the medical footprint in theater. Hence, TATRC decided to fund a pilot project to tackle these challenges. Edward Chaum, MD, PhD at the University of Tennessee Health Science Center and his collaborators at the University of Memphis and Oak Ridge National Laboratory are developing a simple electrochemical method that would permit rapid and accurate quantification of blood Propofol, DIP levels, which can be used as a monitoring method for target controlled infusion anesthesia (TCIA). The organic membrane-coated biosensor, embedded in the catheter, is envisioned to measure the blood Propofol levels and to provide continuous feedback to control drug delivery via the pump.

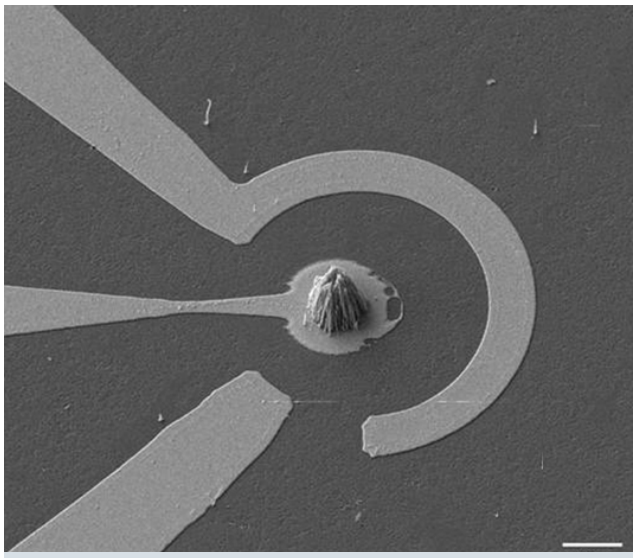


Image of a carbon nanoforest propofol electrode.

Medical Robotics

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Medical Robotics

www.tatrc.org/robotics

The DoD has invested significantly in autonomous vehicles, and other robots to support its Future Force. By leveraging and augmenting funding from these efforts, TATRC has established a portfolio of projects aimed at developing, integrating, or adapting robotic and unmanned ground and air systems to extract battlefield casualties from hostile environments and from under fire. Work continues on a prototype dynamically balanced bipedal Battlefield Extraction Assist Robot (BEAR), which is capable of extracting a 350-pound casualty from various rugged terrains, including urban areas with stairs. Another DoD sponsored project is aimed at exploiting Unmanned Aerial Systems (UAS) to bring sophisticated telemedicine and patient monitoring equipment such as "smart stretchers" directly to military medical first responders and troops engaged in combat. In this arena TATRC is collaborating with Defense Advanced Research Projects Agency (DARPA) to investigate use of UAS to conduct casualty evacuation (CASEVAC) missions and also participating in the North Atlantic Treaty Organization Human Factors & Medicine (NATO HFM)-184 "Safe-ride" Technical Panel convened to investigate safety aspects of such missions.

Other projects are intended to bring telerobotic and near autonomous casualty assessment and lifesaving treatment to the battlefield. These have included the DARPA Trauma pod and several TATRC efforts to integrate robotic arms with the Life Support for Trauma and Transport (LSTAT) litter for robotic implementation of noninvasive technologies such as acoustic cauterization of hemorrhage via High Intensity Focused Ultrasound (HIFU). TATRC has also sponsored research in robotic implementation of Raman spectroscopy and Laser Induced Spectrometry (LIBS) to detect and identify potential chemical and biological warfare agents and explosive hazards to casualties and first responders. Focus is on sensor selection and integration, as well as electronic command and control messaging via the Joint Architecture for Unmanned Systems (JAUS) to include sensors and telemedicine payloads.

In an attempt to generate operational concepts, tactics, techniques, and procedures for implementing medical robotic unmanned systems in combat, as well as the technical requirements to enable those procedures, a computer simulation of the BEAR was created for use in the US Army Infantry Center Maneuver Battle Lab's One Semi-Autonomous Forces (OneSAF) tactical operations modeling and simulation system. An initial series of platoon level assaults and clearing operations in both wooded and urban terrain were executed in OneSAF to include casualty extractions using both conventional litter rescues and rescues with the BEAR. This process has great potential for overcoming the numerous barriers to transitioning research prototypes or new and emerging technologies to operational systems. TATRC FY2009 Projects are summarized below:

The NAVSYS "Tidget" Global Positioning System (GPS)

Zigbee Patient Tracker/Data Logger is a Small Business Innovative Technology Transfer Program (STTR) project intended to develop a wristwatch type GPS tracking system that periodically

NAVYSYS "Tidget" GPS Patient Tracker/Data Logger.

records time-stamped locations of patients being tracked for clinical trials or mass casualty situations. Data can be transmitted to strategically placed servers using the Zigbee communications protocol. The system is also capable of recording time-and-location stamped physiological monitoring data if required.

National Center for Defense Robotics (NCDR) Robotic Manipulator & CASEVAC Mission Software

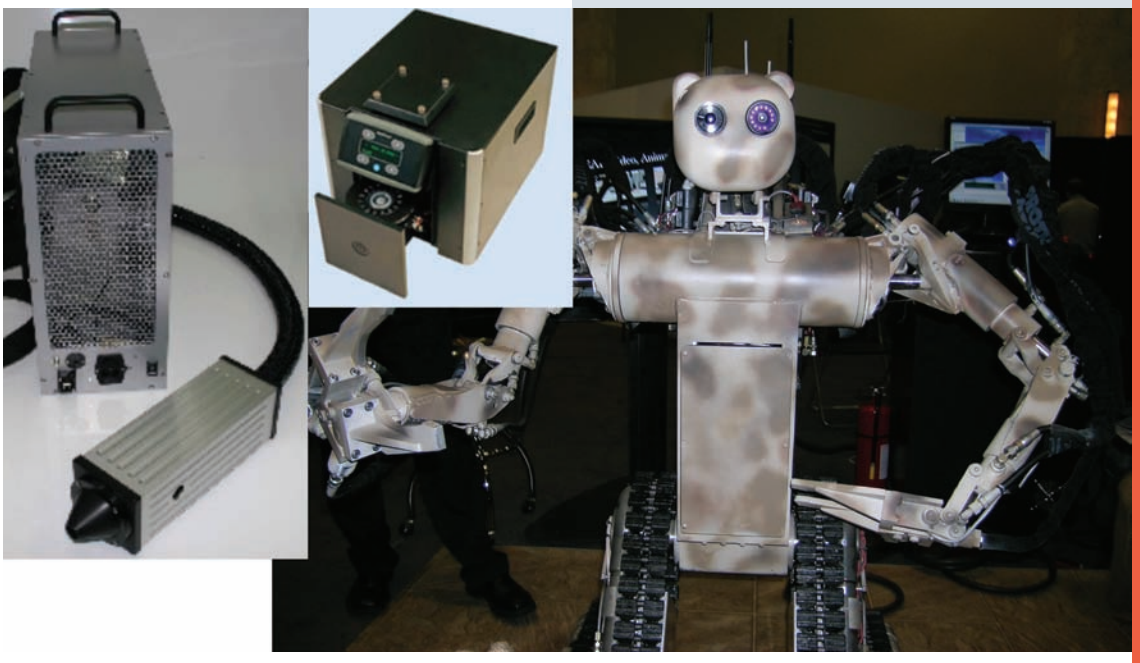
This technology was developed by Applied Perception, Inc., a Qinetic North America company. This was a Congressionally directed research project aimed at adapting the ARES Segway RMP-400 unmanned ground vehicle (UGV) for semi-autonomous casualty rescue and recovery. A robotic manipulator arm, GPS wave point navigation, SIC laser obstacle detection system and stereoscopic cameras were implemented on the ARES UGV, and software was developed and demonstrated for conducting wave point navigation, leader/follower route planning, semi-autonomous casualty extraction via dragging from the Warfighter Modular Lightweight Load-carrying Equipment (MOLLE) gear or towing on a wheeled litter.

ChemImage Robotic Bio Identification Robot (ROBI) Implemented on an ARES UGV

The ChemImage Robotic Bio Identification Robot (ROBI) is implemented on an ARES UGV. This is an Army SBIR project in which Chem-Image has developed a proximity Raman spectroscopy based detector for bio agents and mounted it on the ARES UGV to effect stand-off detection for the operator. An easy to read user interface and an agent library has been developed for bio agents, chemical agents, and explosives as well as commonly found background substances which could interfere with the spectroscopic identification of the threat agents. During 2008, this system was tested at the Army Research Library's (ARL) weapons lab on explosives contained among oil, dust, and other background substances on car door panels and it was able to identify the types of explosives present and successfully distinguish them from background substances.

Vecna Technology Battlefied Extraction Assist Robot (BEAR)

The BEAR project was originally an in-house funded TATRC project aimed at adapting the dynamic balancing technology, also used in Segway platforms, to develop a dual wheeled or tracked humanoid type robot for extracting combat casualties from buildings and hostile environments. Subsequently Congressionally directed and Office of the Secretary of Defense (OSD) Joint Ground Robotics Enterprise has been used to develop a more advanced BEAR featuring separately articulated tracked legs and some degree of semi-autonomy. Vecna Technology Chem/Bio BEAR for Robotic Force Protection from Chem Bio Agents and improvised explosive devices (IEDs). This is an Army SBIR project intended to



Vecna Robotic Chem/Bio detectors for BEAR.

equip the BEAR robot with LIBS and analyte/antigen detection systems for chemical and biological agents and explosives. Vecna is working with Applied Photonics to adapt LIBS explosive detection capability, previously developed for ARL, into BEAR mountable device capable of detecting all three threats. Additionally Vecna is working with IBI to adapt their BioFlash antigen-based bio agent detector for implementation on BEAR.

The Woodward Bewley Alternative Mobile Power Station (AMPS)

This is a TATRC internally funded project aimed at demonstrating generation of electric power using a Proton Exchange Membrane (PEM) fuel cell, fueled by hydrogen, generated from electrolysis of salt water. The initial prototype capability was designed to generate enough hydrogen gas from salt water with a small electrical catalysts generate to power a 100Watts PEM fuel cell. A system prototype was mounted on and integrated with a children's ride-on electrical powered GATOR, such that the AMPS system continually charges the 30 minute battery to enable continuous operation without external recharging.

Anthrotronix Inc. M-4 Rifle Grip & iGlove Robotic Controllers.

This project was a TATRC and Army funded Phase II Enhancement of an ARL SBIR project. The objective was to adapt for BEAR robotic CASEVAC missions, the ergonomic robot operator control

The Anthrotronix rifle grip and glove robotic controllers miminize distractions of their operator's primary combat mission.

Georgetown University's computer assisted interventions and medical robotics.

units originally designed for ARL to enable combat Warfighters to control robotic and unmanned systems using devices that were designed to minimize distraction of the operators from their primary combat mission. The M-4 Rifle grip attaches to the front of the rifle and provides the operator with the capability to control the robot with a joy-stick like device while looking through a side mounted scope. The iGlove enables the operator to control the robot by using standard infantry hand and arm movements coupled with additional finger manipulation controls.

Georgetown University's Imaging Science and Information Systems (ISIS) Center

Georgetown University's Imaging Science and Information Systems (ISIS) Center has been developing robotic devices for computer-assisted medical interventions for the past decade. Originally funded by a Congressionally directed research program entitled Perioscopic Spine Surgery, projects include a needle-driver biopsy robot, a rehabilitation arm exoskeleton, respiratory motion tracking for radiotherapy, a tele-rehabilitation of stroke patients over the Internet, electromagnetic tracking tools used for image guided surgery, and a tele-

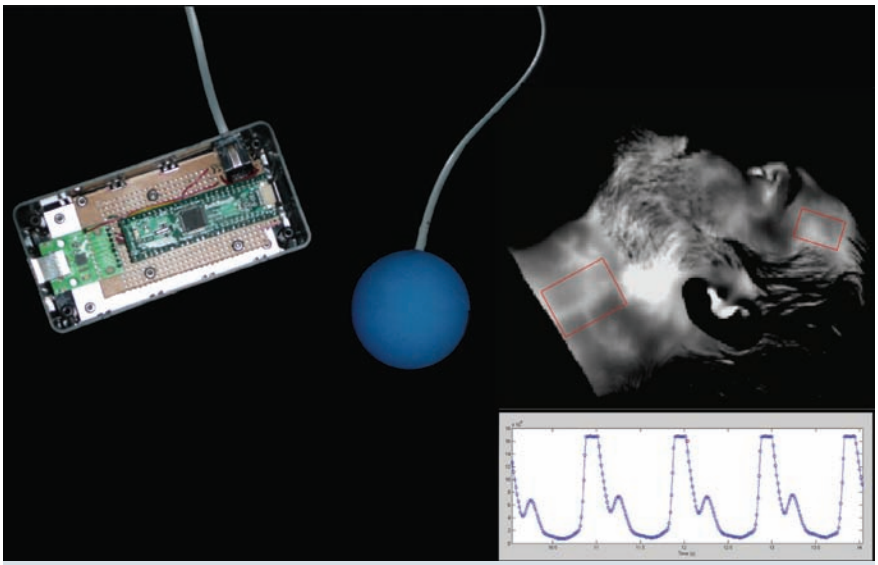
operated robot used for perioscopic spine biopsy procedures.

The H-Star Technologies Robotic Standoff Neck and Spinal Injury Assessment Device

This Army STTR is intended to use C-Ultrasound and infrared sensing systems to detect fractures of the neck, spine and limbs of combat casualties before robotic casualty extraction. In partnership with MIT and Harvard Universities, H-Star intends to develop an imaging system utilizing advanced ultrasound and infra-red imaging solutions that can identify and assess fallen combatants for consciousness and potential head and spine injury, determining those with unstable spine injuries requiring special stabilization requirements during battlefield rescue. The robot base to be used is the Robotic Nursing Assistant (RONA) from another TATRC SBIR aimed at developing a humanoid type robot to assist nursing personnel with patient movement in hospital wards.

The Pearl Research LLC Standoff Remote Triage Sensor Array for Robotic Casualty Extraction Systems

This system is intended to perform standoff triage of combat casualties prior to conducting robotic casualty extraction. This project is using a modular approach for real time remote assessment of combat casualties. It integrates and implements on a robot, the Dynamic Injury Severity Estimation System, the spinal injury assessment sensor and a standoff thermo-imaging system to enable a first responder medic or rescuer to assess vital signs from a remote location.



PEARL Research Remote Robotic Triage system enables a first responder medic or rescuer to assess vital signs from a remote location.

Carnegie Mellon University's serpentine robotic manipulator arm.

The Carnegie Mellon University's (CMU) Serpentine Robotic Manipulator Arm

This TATRC internally funded project is intended to adapt CMU's serpentine manipulator arm and integrate it with the LSTAT as a remotely controlled casualty examination device that enables medics or surgeons to perform tele-examinations on a patient before or during evacuation. A set of noninvasive physiological monitors, developed by TeleMedic from Canada, has been integrated so that they can be robotically placed by remotely manipulating the serpentine arm and a movable gantry device on the LSTAT. With minor modifications, the serpentine arm can be used to perform more complex treatment tasks or could be attached to a small robot for conducting triage during mass casualty situations.

Dragonfly Pictures Inc. (DPI) and Piasecki Aircraft Combat Medic UAS for Medical Resupply and CASEVAC

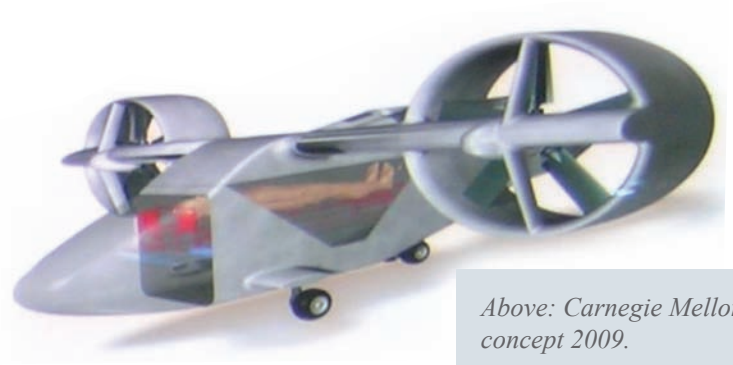
This is an OSD funded SBIR project aimed at developing autonomous take-off, navigation/flight control, and landing for an unmanned aircraft intended to fly into small clearings in wooded terrain and urban canyons for the purpose

of just-in-time delivery of medical supplies to combat medics and potentially for autonomous CASEVAC of casualties. The key research foci of this project are:

- advanced technologies for autonomous UAS take-off, landing, and navigation in urban and wooded terrain; and
- collaboration and coordination between medics and UAS ground crews to effect safe and timely delivery of medical supplies and LSTAT systems so appropriate first responder care and evacuation can be performed during the so called "Golden Hour" of combat casualty care.

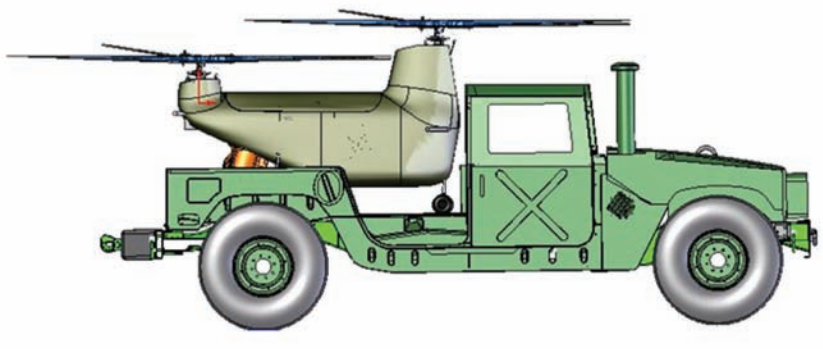
DPI will use its own DP -6 Whisper Demonstrator to demonstrate autonomous flight control, landing and takeoff. A newly designed DP-12 UAS will be used for the final autonomous mission demonstration carrying a 200 lb. payload.

During its Phase II demonstration, Piasecki will demonstrate CMU's autonomous obstacle avoidance, site selection and landing technology using a proven aircraft, the Boeing Unmanned Little Bird. They have developed a unique rotating ladar sensor for effecting unmanned navigation.



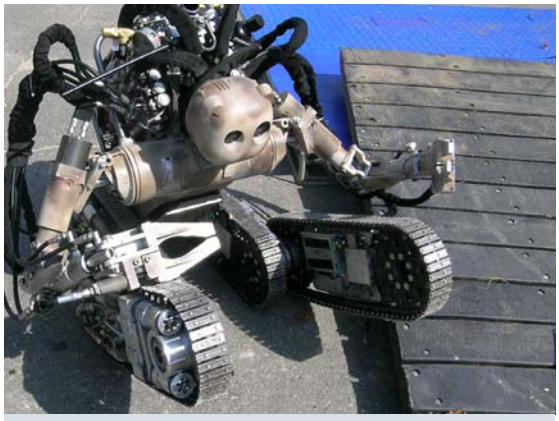
Above: Carnegie Mellon-UAV concept 2009.

Below: RONA Prototype.



Disruptive Transition of Medical Robotic Technologies

This program, a TATRC priority, includes a series of live and simulated user assessments of the BEAR robot that were conducted during 2008-09 at the Fort Benning Infantry Center Maneuver Battle Lab. Traditional military acquisition is a serial process which involves time consuming analysis of gaps in current operational doctrine followed by subsequent investigation of strategies that include, in addition to new technologies, new organizational structures, improved training, and revised leadership techniques. This tedious process often results in technologies which are already obsolete upon fielding and collaboration between their component research and development (R&D) and combat development organizations. As a result, emerging prototype technologies often progress no farther than the laboratory. In order to generate operational concepts, tactics, techniques and procedures for implementing medical robotic unmanned systems in combat, computer simulations of the BEAR and three different operator control interfaces were created in the OneSAF tactical operations modeling and simulation system. These simulations employ both physical and operational models of the BEAR such that during user assessment exercises, the robot operator must fully negotiate terrain obstacles and execute missions within a Battle Lab Simulation Center Computer Aided Virtual Environment (CAVE). An initial series of live and simulated platoon level assaults in both wooded and urban terrain were executed in OneSAF to include casualty extractions using both conventional litter rescues and telerobotic rescues with the BEAR.



The BEAR robot maneuvering up a platform.

Computational Biology at the DoD Biotechnology High Performance Computing Software Applications Institute (BHSAI)

High Performance Computing (HPC)

Advanced applications of high performance computing (HPC) provides the tools for the rapid development of pathogen diagnostic assays and related countermeasures. HPC is transforming the way DoD life scientists design diagnostic assays, and identify potential drug and vaccine candidates against biological warfare agents for force health protection. Instead of relying solely on laboratory experimentation, HPC simulations are now being used to rule out unfeasible solutions and generate testable hypotheses, thereby reducing the number of potential laboratory experiments by orders-of-magnitude, and significantly increasing research efficiencies. What used to take months now takes hours and what used to take years now takes days.

The BHSAI has developed and deployed, at various DoD BHSAI centers, software systems to support design of diagnostic assays and identify drug and vaccine candidates. A few examples of the deployed software systems include:

MAJ Jeanne Geyer of the US Army Research Institute of Infectious Diseases using the TOFI software that helps design microarray assays for pathogen diagnostics. The software is entirely run through a web-browser, making it easier for life scientists without HPC skills to use the system.

- TOFI (Tool for Oligonucleotide Fingerprint Identification) is a software tool for identifying short, unique genome segments of a pathogen's DNA (termed "fingerprints"). The fingerprints are used to design diagnostic assays to identify pathogens of military relevance, such as different *Burkholderia* strains.
- DOVIS (Docking-based Virtual Screening) is a software tool for high-throughput screening of drug-like compounds. Virtual screening guides the identification of chemical compounds that could potentially become drugs.
- PSPP (Protein Structure Prediction Pipeline) is a tool for predicting three-dimensional atomic structures of proteins from their amino acid sequence. Knowledge of protein atomic structures is critical for *in silico* drug screening and vaccine design.

2009 COMPUTATIONAL BIOLOGY FAST FACTS

24 Peer-reviewed journal publications, (14 with collaborations)
HPC Usage: 2,828k CPU-hours

Computational Biology

Portfolio Team

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Dr. Anders Wallqvist
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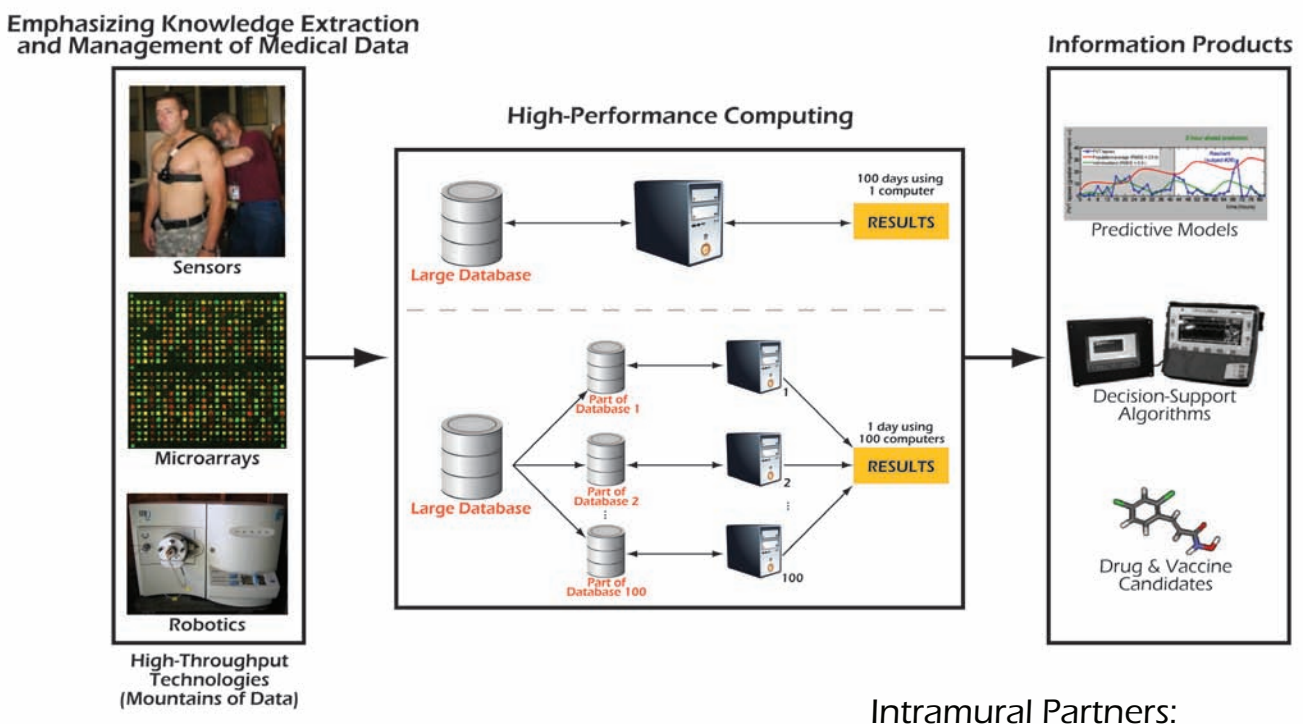
Joy Hoffman
Meri-lyn Ball

and the professional staff of the BHSAI



Data are accumulating at an increasing pace. HPC is needed in order to analyze the large databases, extract knowledge, and allow for the development of mathematical algorithms and models, which are the final products of the collected data.

Intramural Partners:

- USARIEM to prevent heat injuries
- WRAIR to predict impairment due to sleep restriction & develop vaccines
- WRAMC to prevent hypo- and hyper-glycemia in diabetic patients
- USAMRIID to identify drugs and vaccines against infectious diseases
- USAMRICD to design bioscavengers
- NSRDEC to find antimicrobial peptides

- PIPA (Pipeline for Protein Annotation) is a tool for genome-wide annotation of protein functions. Knowledge of the protein functions of sequenced bacteria and viruses is key to the identification of the elements of a microbial genome responsible for its behavior.

Bioinformatics Cell (BIC)

The Bioinformatics Cell (BIC), established by the USAMRMC in 2003, serves as an interdisciplinary resource to develop biomedical computational solutions in support of the Command. The BIC has developed algorithms to quantify the quality of monitored time-series physiologic data; Web-enabled database management systems for large amounts of time-series physiologic data; algorithms to detect hypovolemia in Warfighters with severe injury; and subject-specific biomathematical predictive algorithms, such as Warfighter's core body temperature during physical activity and Warfighter's cognitive state after prolonged periods of sleep deprivation.

For example, on a battlefield and during medical evacuation, combat casualty care is challenging because caregivers may be inexperienced and diagnostic information is typically incomplete. The BIC is developing a platform to provide field-deployable, decision-support tools for patient management through real-time analysis of data from a standard patient monitor via novel "artificial intelligence" algorithms. This is achieved by development and

optimization of a family of algorithms that are intended to accurately identify four key trauma patient conditions: major hemorrhage; respiratory compromise; moderate-to-major TBI; and mortality likelihood. These algorithms rely only on data that are measured by standard patient-transport monitors and will be tolerant of incomplete measurements. The algorithms will be prospectively validated, using our novel "plug-and-play" testing platform, during air ambulance transport of civilian casualties to the Massachusetts General Hospital.

The USAMRMC Bioanalysis Institutes (http://www.bhsai.org), composed of the BHSAI and the BIC, represent a unique model of collaboration between DoD medical research laboratories. No other laboratory within USAMRMC has the scope and breadth of inter-institutional collaboration. In part, this collaborative spirit exists because of the horizontally integrated nature of cutting edge information science, technology, and the increasing recognition of the value of these applications across a wide variety of medical research disciplines.

Publications from basic exploratory science, as well as the use of the HPC tools that have been developed in this group, have soared dramatically within the past few years, since the original inception of this group by Dr. Jaques Reifman.

Software Requests by Outside Organizations*

External Feedback of Software Use

System	Description	Journal Paper Downloads (publication date)	Software Downloads
PIPA	Protein function prediction	1,512 (25 Jan. 2008)	42
CatFam	Protein enzyme prediction	n/a (17 Jul. 2008)	30
DOVIS	Screening of drug-like compounds	3,432 (8 Sep. 2008)	633
TOFI	Design of diagnostic assays	1,528 (21 Oct. 2008)	44
PSPP	Protein structure prediction	n/a (4 Dec. 2008)	44
BNS	Modeling of biochemical cell reactions	1,687 (3 Feb. 2009)	21

* As of 28 January 2010

Representative 2009 BIC and BHSAI Accomplishments

High Performance Computing

• Developed a method to accelerate experimental screening and selection of high-affinity aptamers suitable for small molecule detection using selection of RNA sequences based on secondary structure, generation of a library of 3D structures, and high-throughput virtual screening from the library for desired binding affinities. (Nucleic Acids Res. 2009;37:e87). Collaboration with Air Force Research Laboratory

• Developed a standalone protein structure prediction software package (PSPP) suitable for high-throughput genome-wide structural 3D predictions based on comparative modeling, fold recognition, and ab initio modeling on high performance computing, with a core that integrates more than 20 existing software packages and databases. (PLoS One 2009;4:e6254) (Project download page: http://www.bhsai.org/structure2.html). Collaboration with USAMRIID and Army Research Laboratory

• Modeled the interaction of disordered *Yersinia* effector protein YopE with its cognate chaperone SycE using *de novo* models to generate ensembles of unfolded conformations using REMD simulations and then docking them to the chaperone using a multistep protein docking strategy, suggesting possibilities for chaperone/effector interactions that could be exploited for strategies to interfere with T3SS transport (Biochemistry 2009;48:11158–11160). Collaboration with Army Research Laboratory

• Developed a new method (FIEFDom) to predict domain boundaries of a multidomain protein from its amino acid sequence using a fuzzy mean operator, and demonstrated improvement over six existing sequence-based methods (Nucleic Acids Res. 2009;3:388-395) (an executable of the FIEFDom software is freely available for download at: http://www.bhsai.org/downloads/fiefdom).

• Developed a new method (Cat-Fam) to automatically infer functions of catalytic proteins, which provides >20% additional catalytic functions not inferred by other similarly reliable methods (Proteins 2009;74:449-460)(available at http://www.bhsai.org/downloads/catfarm.tar.gz).

• Constructed a three-dimensional structural model of HuPON1, a human enzyme that potentially could be turned into a nerve gas bioscavenger, and probed binding interactions of HuPON1 with substrates using molecular docking, MD simulations, and binding free energy calculations, identifying key amino acid residues affecting substrate binding, specificity, and postulated catalytic mechanisms, notably residue Y71 (Proteins 2009;75:486-498). Collaboration with Institute of Chemical Defense

• Discovered strategy to improve detection of fluorescence resonance energy transfer (FRET) through the coupling with a synthetic riboswitch (eGFP-REACh), which allows development of more sensitive assay methods (Biomacromolecules 2009;10:1055-1060). Collaboration with Air Force Research Laboratory

• Characterized two key factors (selection of time intervals and number of simulations) affecting the analysis of stochastic simulations to predict the behavior of biomolecular reaction networks (BMC Syst Biol 2009;3:e64). (Project home page: http://www.bhsai.org/bns_alpha.html). Collaboration with Air Force Research Laboratory

• Investigated the effects of temperature and implicit solvents on peptide structure and dynamics using two different models based on the CHARMM22 all-atom force field, finding significant differences between approaches and with better agreement between implicit and explicit solvated peptide dynamics with Langevin dynamics to maintain temperature of the systems (J Phys Chem B 2009;113:12382-12390).

Bioinformatics

• Developed a more accurate method to predict individual performance impairment associated with inadequate sleep, based on a combined strategy that enables model customization as soon as individual performance data comes available and finding optimal estimates from the nonlinear two-process model of sleep regulation (Sleep 2009;32:1377-1392). Collaboration with Department of Behavioral Biology at Walter Reed Army Institute of Research

• Summarized gaps in glucose modeling for closed-loop control from the world leaders in glycemia modeling, highlighting physiological variance as the greatest challenge to creating accurate simulation models (J Diabetes Sci Technol 2009;3:388-395).

• Developed an algorithm for automated analysis of components of pulse oximetry, and heart beat onset and peak from the photoplethymography waveform, that shows promise for detection of hypovolemia (Conf Proc IEEE Eng Med Biol Soc 2009;1:5689-5692). Collaboration with Massachusetts General Hospital/CIMIT (TATRC partner)

• Expanded individualized sleep performance modeling with an approach that also enables estimation of statistically based measures of reliability of the predictions in the form of prediction intervals. (NATO Symposium "Human Performance Enhancement for NATO Military Operations" published as a NATO RTO Technical Report, October 2009). Collaboration with Department of Behavioral Biology at Walter Reed Army Institute of Research.

Representative 2009 BIC and BHSAI Accomplishments

Bioinformatics

• Assessed behavior of linear autoregressive data-driven models developed under three possible modeling scenarios, demonstrating that smoothed data and regularized model coefficients can produce stable and accurate models for near-future (<60 minutes) glycemic predictions (IEEE Trans Biomed Eng 2009;56:246-254). Collaboration with iSense Corporation (TATRC partner)

• Demonstrated that a universal, data-driven model can be generalized to the prediction of subcutaneous glucose concentrations even for patients with different forms of diabetes, based on three studies utilizing different continuous glucose monitoring (CGM) devices and corroborated by Clarke error grid analyses (IEEE Trans Inf Technol Biomed 2009;Oct 23 [Epub ahead of print]). Collaboration with Walter Reed Army Medical Center and iSense Corporation

• Explored diagnostically used temporal trends in prehospital vital signs of hemorrhage, determining that short-term trends are not predictive because of nondirectional fluctuations in vital signs that obscure more subtle progressive trend, especially for high acuity patients, suggesting that increased variability is itself an indicator of acuity (Prehospital Emerg Care 2009;13:286-294). Collaboration with Massachusetts General Hospital/CIMIT (TATRC partner)

• Investigated the diagnostic value of respiratory rate (RR) in respiratory pathology and major hemorrhage using an automated method to compute RR, and showed that RR is as discriminatory as other vital signs when based on data intervals of clean, regular, and consistent respiration during transport of trauma patients, expanding on previous efforts to develop decision support tools in trauma patients during helicopter transport when reliable acquisition of vital-sign data may be difficult (Shock J 2009;31:574-580). Collaboration with Massachusetts General Hospital/CIMIT (TATRC partner)

• Developed a rugged ultramobile vital signs monitoring system which collects numeric and waveform physiologic time series data as a plug-and-play platform for real-time testing of decision-support algorithms during the transport of trauma casualties, and demonstrated that this system can support a quick development cycle for algorithms (Conf Proc IEEE Eng Med Biol Soc 2009;1:3417-3420). Collaboration with Massachusetts General Hospital/CIMIT and Intellisense (TATRC partners)

Systems Biology and Network Science

• Developed a novel computational method to score each pair-wise protein interaction inferred by high-throughput affinity purification methods, and discovered—through analysis of a derived high-confidence network—that the protein interaction maps are highly modular, meaning that the proteins organize themselves into localized, densely connected regions that likely represent individually functioning units (PLoS Comput Biol 2009;5:e1000515).

• Developed a mathematical framework to simulate the quantitative effects on the growth of a pathogen (Mycobacterium tuberculosis) when enzymes in its metabolic pathway are inhibited, based on combining detailed models of a dynamic cell population growth model, enzyme kinetics, and a complete metabolic network description as modeled by flux balance analysis (BMC Systems Biology 2009;3;e92).

• Explored the causes of experimental biases in high-throughput protein-protein interaction networks constructed based on affinity purification methods applied to the proteomes of yeast and Escherichia coli, providing insights into the underlying natures of high-throughput technologies that should lead to more effective strategies for inference and analysis (PLoS One 2009;4:e5815).

Health Information Technologies (HIT)

Health Information Technologies (HIT)

TATRC serves as the Military Health System's (MHS) research arm for emerging and enabling healthcare information technologies and advanced clinical informatics. It manages a portfolio of about 50 Congressional Special Interest, SBIR, and TATRC augmentation funded projects which are typically awarded as grants or cooperative agreements.

Typical research projects involve new human-computer interfaces; clinical decision support algorithms and alerts in electronic health records; revolutionary clinical intelligence tools to facilitate quality assurance studies and clinical research; personal health records; mobile health technologies; new data mart storage technologies; virtualization, cloud, and grid computing; service oriented architectures; terminology and ontology mediation; open healthcare standards and tools; and semantic health information exchange.

HIT is a hot topic, but the question remains whether it can produce real value to the healthcare delivery system. TATRC oversees research to determine how well these technologies can transform health data into information, knowledge, understanding, and wisdom, and to help improve healthcare access, availability, acceptability, cost-effectiveness, continuity, and quality. Many of the projects have the potential to help acquire or access data, analyze or execute data, distribute data, or archive and retrieve data. All are being executed with national and international standards and open source technologies to the maximum extent possible.

If proven to have value, TATRC works with the Military Health System Defense Health Information Management System (DHIMS) and Defense Health Services Systems (DHSS) Program Offices to transfer these technologies into production.

Many of these opportunities are being leveraged, with the concurrence of grant and cooperative agreement recipients, to strengthen existing services, or to build new services in the NHIN, using open source technologies. Examples of the projects follow.

"Like our DoD/VA sharing solutions, the NHIN will enable health information to follow the patient, ensuring it is available for clinical decision making, and supporting appropriate use of health care information beyond direct patient care."

Mary Ann Rockey, Program Executive Officer and Deputy Chief Information Officer (Acquisition) for the Military Health System

HIT FAST FACTS FY09

- $81M research projects
- 31 Congressional Special Interest
- 18 SBIR and other special funded projects
- 8 AAMTI
- 3 Cooperative Research and Development Agreements (CRADAs)

Portfolio Team

LCDR Steve Steffensen
Tom Bigott
Robert E. Connors
Mark Jeffrey
Rob Sharma
Joe Longo
Jerry Goodnough
Kim Pham
Chrisjan Matser
Dr. Doug Fridsma
John DePasquale
Curtis Callender
Marco Konzer
Jordana Thomas
Crystal Ferrell
Kelby Conley
Caroline Gibson

HIT Key Research Project Categories

Acquisition-Access

• Refers to projects that can either assist with combining large disparate data to allow access to actionable information, or projects that capture computable data in new ways. Examples include new human-computer interfaces that can facilitate novel data entry, such as speech recognition, natural language processing, and electronic paper and digital pens

Analysis-Execution

• Refers to projects that analyze or use novel tools to allow analysis of large amounts of information to find patterns or relationships among data sets. These technologies may also predict certain events or conditions or analyze data to optimize scheduling or resource allocation. It also refers to technologies that allow creation, storage, management, and execution of clinical guidelines and rules to assist decision making (e.g., clinical decision support).

Interoperability-Standards

• Refers to projects that help promote interoperability between systems (particularly semantic interoperability and computability) or help define, harmonize, and implement recognized health information technology standards.

Distribution-Portability

• Refers to projects that distribute information or make information portable (both software and hardware) across all spectrums of care, and across the life of an individual.

Representation-Visualization

• Refers to projects that develop novel ways to represent or visualize data or processes. Examples include novel graphical user interfaces, new 3D graphical technologies, virtual world technologies, technology that may improve how providers can abstract increasing amounts of data, display data based on a problem orientation or any novel methods that will increase decision making or improve cognitive performance to allow a more holistic and systematic management of a patient. These technologies can also provide a way to integrate and provide instant access to a comprehensive view of each patient that includes images, scanned documents, proteomic/ genomic, and other clinical observational data.

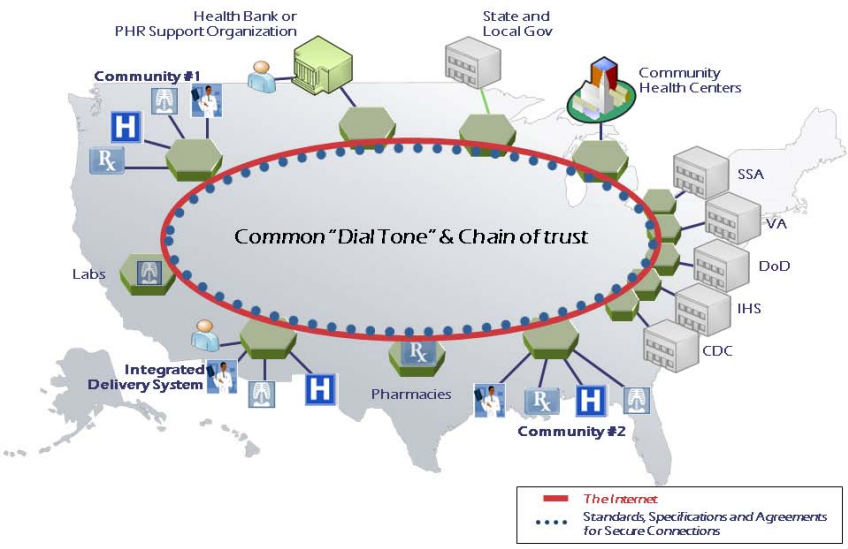
Archive-Retrieval

• Refers to projects that demonstrate methods of archiving data and/or retrieving data in novel more efficient ways. It should handle large sets of data distributed over large distances. (may include data warehousing, data modeling, extraction, transformation and load functions, etc.)

Connecting Relay Health to the NHIN Prototype

This program has become a national priority. As part of a Congressional Special Interest Project, Hospital of the Future, awarded to Spartanburg Regional Health System, SC, TATRC partnered with RelayHealth, Inc. to connect RelayHealth's secure messaging and personal health record platform to a prototype NHIN CONNECT Gateway. The partnership was an opportunity that became possible because Spartanburg Regional Health System uses the McKesson Electronic Health Record (EHR) in their facility, and wanted to explore use of the RelayHealth services. RelayHealth, Inc., a subsidiary of McKesson, Inc., pioneered online healthcare communications to improve the delivery and accessibility of healthcare. It provides connectivity that allows physicians to efficiently, affordably, and securely communicate with their patients. The NHIN is being built to provide a secure, nationwide, interoperable health information infrastructure that will connect providers, consumers, and others involved in supporting health and healthcare. The NHIN will enable health information to follow the consumer, be available for clinical decision making, and support appropriate use of healthcare information beyond direct patient care so as to improve health. RelayHealth service was also integrated into the McKesson EHR at Spartanburg Regional Health System. If brought to production, RelayHealth would become a "citizen of the NHIN," and its secure messaging and Personal Health Record services could be available nationally.

The NHIN: "A Network of Networks"



HL-7 Info Button Services in NHIN

TATRC is overseeing a Congressional Special Interest project awarded to Healthwise, Inc., whose nonprofit mission is to help people make better health decisions. Healthwise, Inc. provides patient education material under a concept known as Information Therapy (Ix®).

With Healthwise Information Therapy, hospitals, health plans, and disease management companies can give consumers the right information at just the right time, to help them make better health decisions. Healthwise, Inc. believes that information is as powerful as any test, medication, or surgery, and that without it, medical care is incomplete. Under the Congressional Special Interest Project, Healthwise, Inc. is working to place Health Level Seven (HL-7) Info Button Standard services into the NHIN in an open source manner. The implementation will allow clinicians to request patient information from HealthWise, Inc., or other content vendors, or to attach such material to a document transiting the NHIN.

TRICARE Health Information Exchange (THIE)

A Congressional Special Interest Project established a TRICARE Health Information Exchange (THIE) in Pensacola, FL to share protected health information (PHI) between Sacred Heart Healthcare System and Naval Hospital Pensacola. The Health Information Exchange (HIE) is made possible through the implementation of Cogon Systems' Virtual Health Network (VHN), which is linked to the DoD/Veterans Health Administration (VHA) Bi-Directional Health Information Exchange (BHIE). The following data set can currently be accessed transiently by military and civilian providers via web services:

- C32 limited data set
- Medications
- Patient demographics
- Laboratory Results
- Diagnoses/Problem List
- Radiology results
- Providers
- Clinical notes
- Allergies

PHI data exchange began on 12 June 2009. As of June, 46,752 civilian records were announced to the BHIE platform with 6,144 records having a cross-correlation to MHS record. An economist will measure the impact of the exchange on avoiding otherwise duplicate tests which would be ordered in lieu of an operating exchange.

In collaboration with the Pensacola Bay Chamber of Commerce, Strategic Health Intelligence, LLC (SHI) was established with the involvement of major civilian healthcare providers and Naval Hospital in Pensacola. The intent of SHI is to foster health innovation and to sustain the health information exchange in Pensacola as a public utility.

Although this project has been successful, it provides a point-to-point exchange between a DoD facility and a civilian healthcare facility which will be avoided in the future due to cost maintenance issues. In the future, DoD and VHA facilities will employ the NHIN CONNECT Gateway to connect to the NHIN, and exchange information with civilian facilities via the NHIN.

INRange, Inc., TelePharmacy Robotic Medication Delivery Unit (TRMDU)

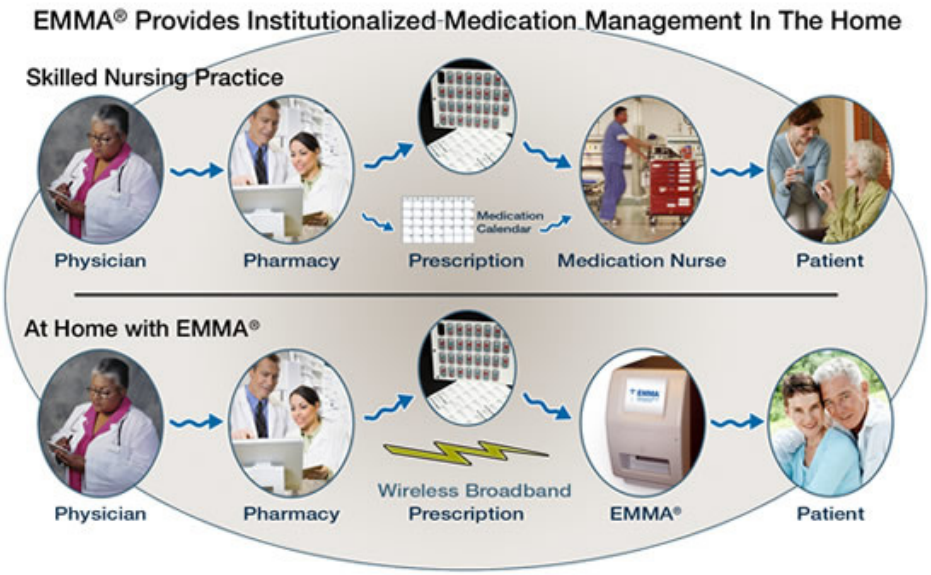
This pilot project tests a Remote Medication Management Device at a Naval Hospital, Camp Pendleton, California, Ireland Army Community Hospital, Fort Knox, and VHA Tampa. The device is already implemented in transient units at WRAMC. Commercially, the product is known as EMMA®. The device is intended to improve medication administration. Past research suggests that 60% of patients do not adhere to their prescribed medications for multiple reasons. This project will determine if EMMA® can improve patient adherence to taking prescribed medication.

The EMMA® system consists of a Medication Delivery Unit (MDU) and wireless two-way web-based communications software that allows a physician, pharmacist, or other licensed practitioner to remotely manage prescriptions stored and released by the patient-operated MDU. The patient's prescriptions and refills are packaged in standard-sized blister cards which are dispensed to the patient in place of an amber bottle filled with pills. Each MDU can hold up to 10 blister cards (multiple blister cards may be connected together) that are loaded into the MDU much like CD's are loaded into a car or home stereo. The MDU identifies each medication automatically—no patient input is required. Changes made to the dosing instructions are transmitted to the MDU—no home nursing visit or physician phone instructions are needed.

When it is time for the patient to take their medications, the MDU emits an audible and visual alert to the patient. When activated by the patient, the medications are selected from the blister cards and released into the delivery tray.

EMMA® is the first and only device cleared by the FDA for use in Remote Medication Management. When programmed remotely by a pharmacist or other licensed professional from their pharmacy or office, EMMA® then delivers the medications to the patient or a caregiver without the need for a licensed professional to verify that each dose is correct.

TATRC is piloting InRage, Inc. EMMA® remote medication management units for use in Wounded Warrior Transient Units.



Clinical Looking Glass, "A Revolutionary Clinical Intelligence Tool"

TATRC is working with Emerging Health IT, Inc. (Montefiore Medical Center, NY), to pilot a revolutionary clinical intelligence tool known as the Clinical Looking Glass. This is currently used by clinicians at Montefiore Medical Center to perform quality assurance studies and health research studies. Clinical Looking Glass is a data warehouse with an easy to use front end that allows clinicians to build study and control cohorts at their desktops, using data from the electronic health record, and make comparisons between these groups as to differences in health outcomes. Cohorts can be compared on-the-fly with statistical measures graphical outputs ready for use in quality assurance meetings and publications. All of this is done automatically, in a matter of minutes, with no need for chart

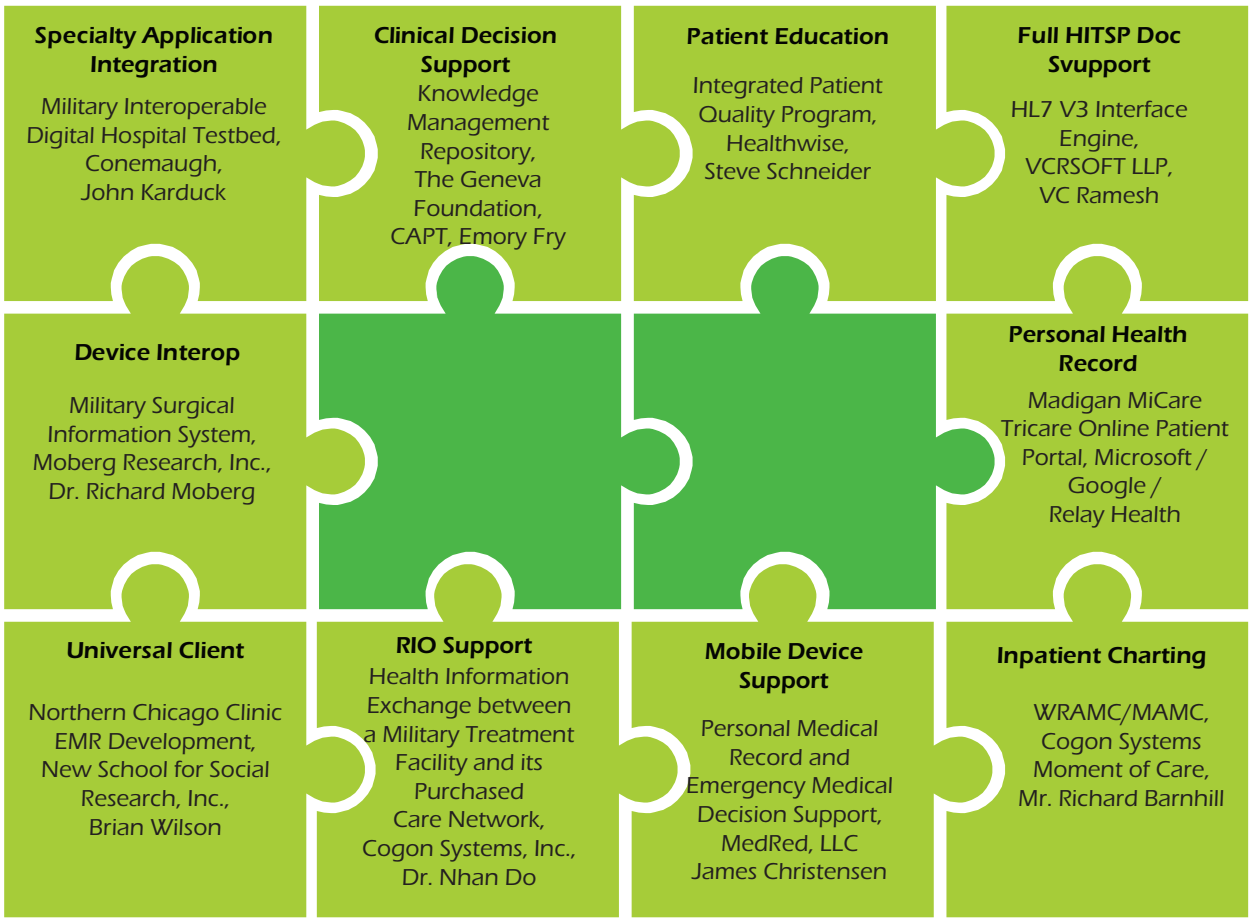
abstracts, or statisticians. All cohorts and results can be saved as objects for resuse and sharing with colleagues. By default, all studies are done with de-identified data; however, identified data is available to those with permission to support patient remediation at the point of care.

Between 2006 and 2008, TATRC established the Clinical Looking Glass with de-identified data from the National Capital Area. In 2009, TATRC began establishing a pilot of the Clinical Looking Glass at the US Air Force Population Health Center, Brooks City, TX. The plan for 2010 is to feed the Clinical Looking Glass with MHS data from the Air Force Corporate Health Information Processing Service (AFCHIPS) warehouse, and then make the Clinical Looking Glass available for further evaluation by select clinicians at National Naval Medical Center (NNMC) Bethesda and Walter Reed, over the web. Given a successful pilot at Brooks City Base, clinician support, and funding, the plan is to move Clinical Looking Glass to production as a system of record for the MHS.

TATRC Managed and Funded Projects for the NHIN

The NHIN, led by the HHS National Coordinator for Healthcare Information Technology, is an important national priority to establish an interoperable HIE. The adoption of the NHIN by clinicians, group practices, health maintenance organizations, insurance companies, and local and regional health information exchanges will depend on the existence of value-added information exchange services within the NHIN architecture. While the NHIN's initial focus is on exchange of Healthcare Information Technology Standards Panel (HITSP) C.32 Summary of Care Documents, the NHIN is more than a medical records exchange, serving a broader health

TATRC Managed Congressional Special Interest, SBIR, and Augmentation Funded Projects which are Contributing to Strengthening Existing Services or Building New Services in the NHIN.



information exchange. Desirable candidate services in the NHIN might include:

- Specialty Application Integration
- Clinical Decision Support
- Patient Education
- Full HITSP Document Support
- Device Interoperability
- Personal Health Records
- Universal Client, Mobile Device Support
- Regional Health Information Organization Support
- Inpatient Charting

Previously, TATRC's main role was to oversee Congressional Special Interest, SBIR, and other augmentation funded efforts. During the pre-award process for these projects, TATRC works with the recipients of this funding, and where appropriate, and with the concurrence of the recipient, shapes the recipient's proposal to build new services or strengthen existing services in the NHIN, as shown in the diaagram.

As one example, TATRC oversaw a Congressional Special Interest Project awarded to COGON Systems, Inc., which built a working, point-to-point health information exchange between Naval Hospital, Pensacola, and Sacred Heart Health System using the DoD/VHA Bi-Directional Health Information Exchange, and COGON's Moment of Care Exchange. The work was aimed at establishing an exchange that would reduce unnecessary lab tests for shared patients. In the process of developing this exchange, TATRC learned much about the limitations of BHIE to semantically constrain data for use in the NHIN, and another set of web services and adapter was developed by TATRC to better support connections of the Armed Forces Health Longitudinal Technology Application (AHLTA) to the NHIN.

TATRC is also working with Conemaugh Health System. A small portion of this project funding was used to help build the federal adapter for the NHIN. Conemaugh is currently implementing a commercial EHR across their system, and will soon move to connecting to the NHIN. Once connected, information could be shared among Conemaugh, the VHA and military benefiaries in the area.

As another example, TATRC worked with Healthwise, Inc. to build an open source HL-7 InfoButton Services prototype for the NHIN. The service allows a clinician to ask for patient education material, to be delivered by Healthwise, Inc. or a competitor, to the point of care, using the NHIN infrastructure.

TATRC oversees a project with Parsons Institute for Information Mapping, which is examining alternatives to improve the human-computer interface for electronic health records, and create a universal client. This work may prove useful to both AHLTA, VistA, the NHIN, and the joint DoD/VHA facility at North Chicago.

Working with Moberg Research under a SBIR grant, TATRC is exploring how to improve communications among surgical information system components, improve medical device interoperability, and integrate clinical decision support, using the NHIN infrastructure.

TATRC is also working with VCRSoft, Inc., to determine how to improve semantic interoperability and decision support capabilities within the NHIN. Some of the work has examined methods to convert HL-7 3.0 Continuity of Care Documents (CCD) to Continuity of Care Records (CCR) and vice versa, so as to promote exchange of information. Other aspects of the work have researched use of open source HL-7 interface engine, known as Mirth. Recently the project has focused on how a population-based Virtual Medical Record like HL7 V3 RIM compliant information and data model can be used to support reporting of performance measures and metrics based on the Indian Health Service (IHS) Clinical Reporting System (CRS).

Additional significant work in Clinical Decision Support is being accomplished through a project by CAPT Emory Fry at Naval Health Research Center (NHRC), on clinician-centered evaluation of the usability of AHLTA and automated clinical practice guidelines with a clinical decision support (CDS) Knowledge Repository.

CDE support for the NHIN

Over the past three years, TATRC has developed the Common Development Environment (CDE) which consists of a Software Development Environment (SDE) and an Operational Test System. The SDE provides secure distributed software development and fast prototype testing environment capable of supporting multiple software development projects simultaneously utilizing a virtual machine (VM) environment. The Operational Test System is an exact replica of the fielded AHLTA system to include the latest software and database patches and updates which insures all final testing is performed against an exact replica of the live AHLTA system. Combined, the SDE and the Operational Test System enable TATRC staff and third party developers to test and develop in a safe, sand box like environment without touching the live operational system.

TATRC software engineers developed the NHIN-Adapter utilizing a VM which supported its development and testing, as well as, hosting a copy of the Federal Healthcare Architecture (FHA) NHIN Gateway. The NHIN Adapter accessed the TATRC developed Patient Ancillary Web Services (PAWS) on the CDE SDE which is linked to the Operational Test System with a Central Data Repository (CDR) containing out-patient test data. When the TATRC NHIN Team completed their work on the Adapter, all their software code and documentation was passed on to Northrop Grumman.

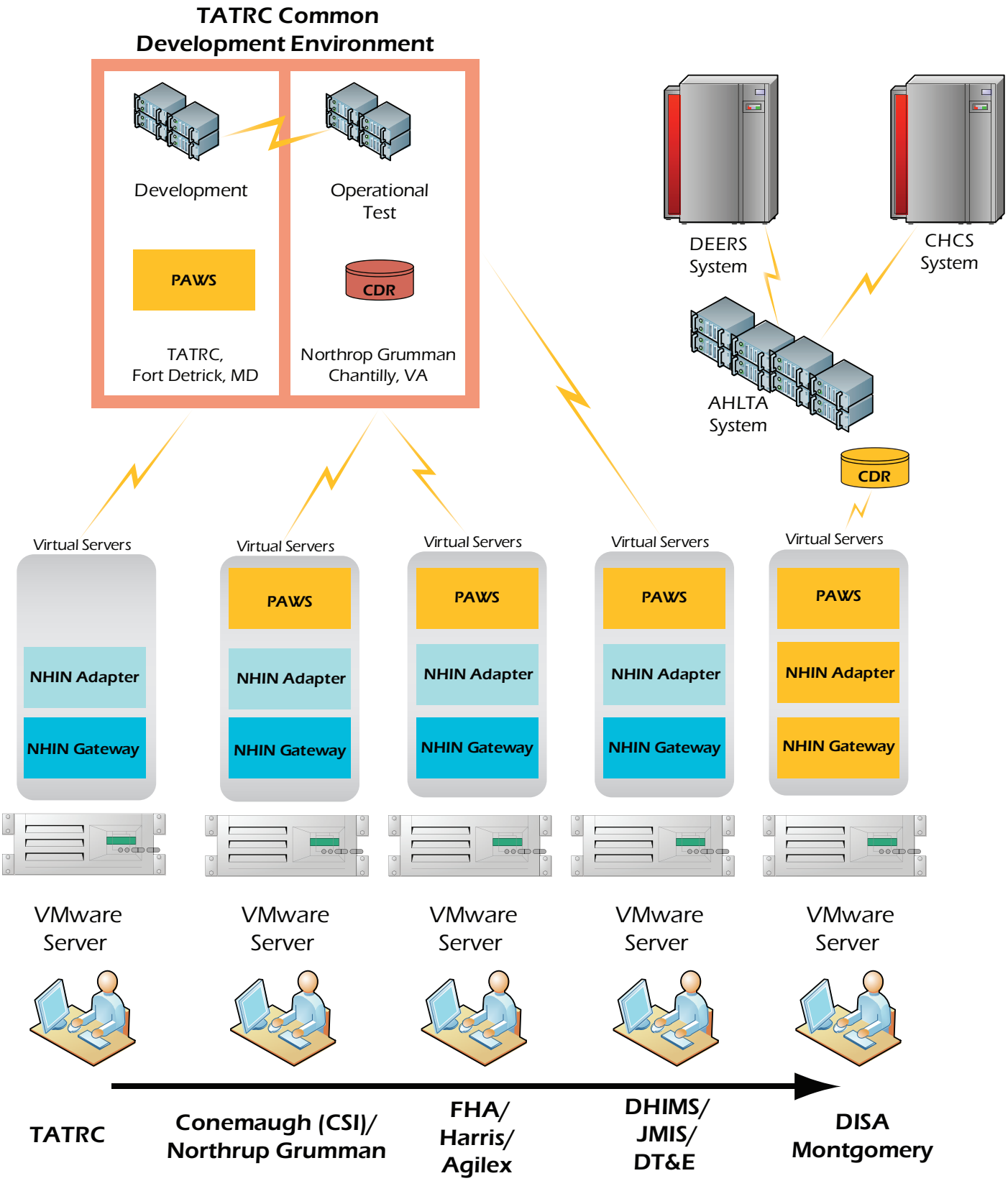
Northrop Grumman was responsible under the TATRC Conemaugh Congressional Special Interst contract to update the Adapter's Common Access Layer (CAL) and test the complete NHIN system utilizing a VM supporting the PAWS, Adapter, and the Gateway virtual servers accessing the TATRC Operational Test System. Upon Northrop Grumman's test completion, all software code and documentation was passed on to the FHA.

The FHA contracted with Harris Corporation who subcontracted with Agilex. FHA productized and tested the entire system ensuring it met the DoD Information Assurance Certification and Accreditation Process (DIACAP). Utilizing a VM, the three virtual servers were again tested utilizing the CDE Operational Test System. Working with the DHIMS/Joint Medical Information System (JMIS)/ Development Test and Evaluation (DT&E) Center, the FHA conducted joint testing to ensure the NHIN passed all testing and security requirements. When all testing was complete, all software code and documentation was passed to the Defense Information Systems Agency (DISA) in Montgomery, AL.

DISA is responsible for AHLTA, the complete live operation of the DoD out-patient EHR. AHLTA supports over 9.5 million active duty and retired military and family members and has system interfaces with the Defense Enrollment Eligibility Reporting System (DEERS) and the Composite Health Care system (CHCS) providing patient appointments, medications, and laboratory management support. Utilizing a VM, DISA has tied the NHIN System into the AHLTA production environment.

The development and implementation of the NHIN would not have been possible without the direct support of TATRC staff and the CDE. The operational deployment of the NHIN Phase 1a in San Diego, CA was the first of many deployments in support of the presidential directive for a VLER.

CDE Support for the NHIN



Key Accomplishments (since 2006)
Health Information Technology Portfolio (HIT)

Accomplishment	Military, Local, State, Regional and National Impact
• Created the TATRC Common Development Environment (CDE) for development and testing of new applications with DoD AHLTA Electronic Health Record (EHR), the Nationwide Health Information Network (NHIN), and Virtual Lifetime Electronic Record (VLER).	• Provides the Military Health System (MHS) with a development and test capability for the electronic health record. This capability was critical to the development of the first phase of the high visibility NHIN/VLER project.
• Contributed to the development of the NHIN, which is under the control of the HHS National Coordinator for Healthcare IT, by leveraging seven major Congressional Special Interest projects at TATRC, and shaping them to build new services or strengthen existing services. • Designed and developed software federal adapter for the NHIN, which connects NHIN CONNECT Gateway to back-end federal and commercial medical systems, to promote standards-based exchange of health data. • On behalf of MHS CIO, coordinated NHIN production pilot software development to exchange a HITSP C.32 document between Naval Medical Center, San Diego, VAMC San Diego, and Kaiser Permanente. • Created Patient Ancillary Web Services (PAWS) as robust means of pulling data from AHLTA Clinical Data Repository to support numerous third party applications requiring that data. • Funded a working, production exchange between Naval Hospital, Pensacola, Florida and Sacred Heart Health System, which exchanges laboratory data using the DoD/VHA Bi-Directional Health Information Exchange (BHIE) and the COGON Systems Moment of Care Health Information Exchange. Project resulted in identifying limitations in the ability of the DoD/VHA BHIE to semantically constrain data and be NHIN-compliant and identified cost challenges in point-to-point health information exchange. • Prototyped connection of McKesson Relay Health Secure Messaging and Personal Health Record (PHR) as a service on the NHIN. • Engaged Healthwise, Inc. to prototype open-source HL-7 InfoButton Service for the NHIN. Provided thought-leadership to ongoing government legal review of open source software issues.	• Accelerates the President's goals for NHIN/VLER and contributes key components (federal adapter and common access layer) for the production NHIN/VLER. This sets the stage for more efficient exchange of healthcare summary data between DOD, VHA, and civilian healthcare institutions.
• Conducted TATRC speech recognition pilot study of Nuance Dragon Naturally Speaking, Medical, for garrison and theater use.	• Accelerated adoption of speech recognition by interested clinicians, resulting in improved ease of data entry into AHLTA and increased patient through-put, supporting a key element of the Army Surgeons General's MAPS Program for improved AHLTA Provider satisfaction.

Key Accomplishments (since 2006)
Health Information Technology Portfolio (HIT)

Accomplishment	Military, Local, State, Regional and National Impact
• Evaluated reliability of natural language processing engines, and developed prototype implementation of natural language processing engine in AHLTA to automatically provide structured coded concepts and facts for use in evaluation and management coding, clinical decision support, pharmacovigilance, and biosurveillance.	• Positions a commercial NLP engine for insertion into production AHLTA, similar to Kaiser's implementation of Language and Computing's engine on top of Epic, a commercial EHR. NLP is a sophisticated computer technology, which turns free text into coded concepts and facts (supported by SBIR program).
• Piloted a Revolutionary Clinical Intelligence Tool, Clinical Looking Glass, developed by Montefiore Medical Center, Bronx, NY, with Military Health System data. Establishing production grade pilot at US Air Force Population Health Center to support Military Health System quality assurance, translational medicine, and patient remediation at the point of care.	• TATRC's prototype work has positioned the Clinical Looking Glass tool for production, given additional funding. There is no similar tool currently in the MHS Automated Systems Inventory which allows a clinician to easily build study and control cohorts for quality assurance studies, and compare these groups to differences in outcomes using advanced statistical measures.
• Executed CRADA with Intel, Microsoft, and Hewlett Packard, which built and demonstrated a new $1M clinical data mart prototype at Madigan Army Medical Center, using a different approach to data storage and access (Kimball's fact and dimension modeling).	• The MHS DHSS Program Office, and its sub-contractor, ASM Research, Inc., incorporated certain aspects of the TATRC/Madigan work and data model into the new clinical data production system which was recently released.
• Established Military Health System Data Mining Algorithms through contract with KBSI, Inc. which discovered previously undiscovered important relationships in MHS data, and advanced the concept of an Advanced Clinical Research Information System (ACRIS).	• This work formed the basis for the concept of a separate and dedicated research data cube (ACRIS), which combines clinical and business information, and is supported by advanced data models, OLAP, and true data mining tools (discovering previously undiscovered knowledge in MHS data using pattern recognition). The current data warehouses are over-taxed with operational demands). The concept is pending sustained funding and implementation under a Health Research Center at TMA, or the Uniformed Services University.
• Advanced DOD Pharmacovigilance efforts through an agreement with e-Health Initiative, a public-private consortium to use military health data to study post-marketing drug surveillance.	• Through this agreement, the MHS used its data to validate several post-marketing drug surveillance use cases presented and also garnered additional staffing support to the Army Office of the Surgeon General for DoD pharmacovigilance.
• Implemented demonstration project to establish remote medication management (InRange EMMA units) at a major Marine Corp base with expansion of the project planned.	• These systems will provide scheduled medication drops for TBI and PTSD patients in transient units, improving patient safety, reducing adverse events associated with polypharmacy, and allowing closer monitoring of patients' medications.
• Worked with several recipients of Congressional and SBIR funding to prototype improved graphical user interfaces to AHLTA (Stottler Henkle, Inc. time display of data; SSCI, Inc. POINT display of context sensitive, clinically-relevant data; Parsons Institute for Information Mapping; Conemaugh Medical Center).	• This prototype work, if implemented in the DOD AHLTA Electronic Health Record, could significantly improve clinicians' visualization of data and potentially improve patient safety and quality of care. It can also improve clinicians' use and acceptability of AHLTA for documentation of clinical encounters.
• Provided several million dollars of direct system analysis support to the TRICARE Management Activity, using a Congressional Special Interest Project with Deloitte Consulting, to create requirements and concepts of operation to transition from a paper to digital record. • Oversaw prototype of a state-of–the-art scanning system from KYOS, Inc. that automatically indexes documents for retrieval.	• This work was critical in the development of requirements for the Health Architecture Imaging Managing System (HAIMS), which will store a variety of digital imaging studies and documents, including healthcare consults reports from civilian medical facilities. These images will then be available in AHLTA to help improve healthcare delivery decisions.

Medical Imaging Technologies

Medical Imaging Technologies

Standardizing Imaging Techniques

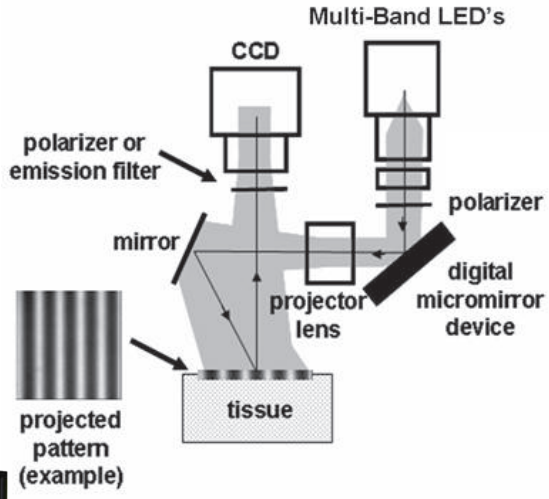
In order to take advantage of the power of imaging techniques, experts in the fields of Magnetic resonance imaging (MRI) and Radiology have come to realize the need for standardizing common procedures for both diseases and trauma. While the need for standardizing clinical protocols across institutions for routine diagnoses has been noted almost since the inception of modern imaging, much remains to be done to eliminate confusion between physicians at different institutions. This problem gains more importance everyday, as the number of referrals for medical imaging procedures steadily increases.

The prevalence of TBI in the current conflicts has reinforced the need for standards related to data acquisition, post-processing and archiving. Standards for data acquisition and post-processing have gained increasing military relevance as they are critical dimensions of cutting-edge neuroimaging techniques such as Diffusion Tensor Imaging (DTI).

Developing acquisition and post-processing standards for DTI remains a critical roadblock against adapting this technique into the clinical as part of the standard-of-care for our injured service members.

Developing clinical standards for imaging will enable easier interpretation of results and could be used to optimize radiation exposures for techniques such as computed tomography (CT). Most importantly, it could lead to large, comprehensive databases that would dramatically improve our understanding of disease and trauma.

Dr. Faina Shtern of the Admetech Foundation has worked hard for a solution to identify new strategies for detecting and diagnosing prostate cancer at its earliest stages. Thus far, the



Left: Technology such as SEAtreat™ photodynamic therapy (PDT) Clinical Instrument enables better selectivity to determine cancer margins and the ability to customized.

Above Right: PDT System Architecture allows for PDT dose optimization through the continuous monitoring and adjustment of the PDT light dose during treatment.

Portfolio Team

Dr. Anthony Pacifico
Ron Marchessault
John Day

work of her co-investigators has resulted in the discovery of numerous leads leads for new biomarkers. More recently (2008-2010), Dr. Shtern has redirected the work of the foundation toward the development of an MRI working group. The working group has two functions:

- Expedite testing of MRI/Spectroscopy (MRI/S) for diagnosis and assessment of treatment for prostate cancer; and
- Develop near- and long-term research strategy for facilitated advancement of MRI/S for prostate cancer.

Both of these goals are planned to be coordinated amongst experts at leading prostate cancer research centers. It is hoped that the large consortium of established prostate cancer investigators will reach a consensus regarding the application of MRI/S for prostate cancer diagnosis. This consortium represents a new way to develop efficacious imaging strategies for diseases as it minimizes competition between institutions.

Dr. Michael Vannier of the University of Chicago attacks a similar problem. Dr. Vannier is a well established MRI physicist and is faced daily with issues related to brain trauma at his clinic. This is a problem that has become increasingly prevalent in the military due to the ongoing conflicts. There are a number of state-of-the-art techniques available for diagnosing these injuries in various stages of clinical validation. In order to bolster to the strengths of ongoing research in DTI, Dr. Vannier has planned as series of conferences and workshops intended to bring the community of DTI researchers and clinicians together. There is an immediate need for these meetings as this new technique has great potential associated with it for diagnosing diffuse axonal injuries, a form of debilitating neurological insults. Standards and conventions regarding data acquisition and processing are required and will enable this community to efficiently share data, therefore exponentially increasing the power of their studies.

Clinical Studies with State-of-the-Art Imaging for TBI

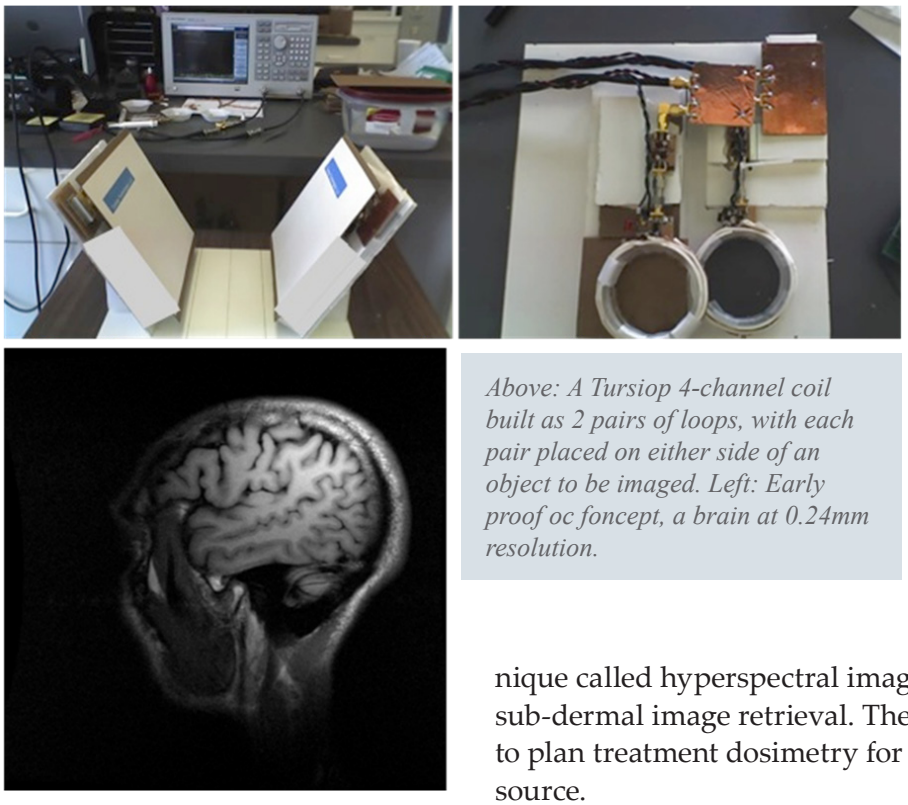
There is a need for early phase high impact clinical stuides with state-of-the-art imaging techniques for TBI. This work is needed, as it will develop principal hypotheses for future work that brings science to practice. Perhaps the largest challenge for these small studies is identifying and developing clinical protocols and endpoints relevant to the cognitive, psychological and motor deficits seen in servicemembers returning from combat. In addition to developing and modeling the complicated physics of newer techniques such as DTI, the very essence of how these injuries are sustained remains a challenge with respect to our understanding of trauma. Developing clinical trials that test militarily relevant hypotheses with these new techniques is critical. Furthermore, these hypotheses need to be grounded in widely accepted testing techniques used by experts in psychology, cognition, and physiology.

The solution involves understanding the nature of the cognitive, physiological, and psychological deficits that have stemmed from brain injuries. This has been an intense focus for military healthcare providers almost since the start of the current conflicts. Military organizations such as TATRC have come to realize the strength of partnering with academic institutions to yield high-quality data and research to improve the care and rehabilitation of our injured service members. As a result, TATRC is supporting several investigators in high performance imaging with the goal of developing and translating cutting edge imaging modalities into the clinic for our troops.

Dr. Richard Linton of the University of Oregon has developed a multidisciplinary team of investigators to improve neurorehabilitation for patients with acute brain injuries. Dr. Linton's group has adapted functional MRI methods with the goal of neurorehabilitation related to traumatic brain injuries using an innovative strategy for combining dense array electroencephalogram (EEG) data with functional MRI data for treatment planning related to seizures. The technology has been successfully used in humans and awaits further evaluation. It is hoped that the functional MRI data could be eventually supplemented by other data from DTI, for example.

TATRC is also funding efforts that combine imaging with new strategies to detect manifestations of post-traumatic stress disorder (PTSD). In collaboration with Gina Forster of the University of South Dakota, TATRC is working with new and innovative ways to monitor individuals for PTSD in order to assist with their rehabilitation.

One of the biggest challenges with translating DTI into the clinic is accurate representation of the fibrous tracts of the brain. Accurately assessing diffuse axonal injuries will dramatically improve our understanding of the basic mechanisms of TBI. Dr. Stephen Rao and his team of researchers are working on new methods to discern axonal breaks, bends, crossing and stretching to provide a better assessment of the level of injury for each patient. Furthermore, Dr. Rao and his group will extend their axonal research into developing accurate fiber tract maps, which will be correlated to brain activity.



Above: A Tursiop 4-channel coil built as 2 pairs of loops, with each pair placed on either side of an object to be imaged. Left: Early proof oc foncept, a brain at 0.24mm resolution.

Medical Imaging Devices

Another problem stems from conventional medical imaging modalities which currently revolve around MRI/S, Ultrasound or Radiographic techniques. While each of these has added significant value to healthcare today, none of these techniques singlehandedly reveals complete details regarding a patient's physiological status. Secondly, use in rural environments and the battlefield is nearly unheard of for MRI due to cost and weight concerns, and thus limited to radiographic techniques such as x-ray. While ultrasound is highly portable, it is sensitive to artifacts, the images can be hard to interpret and the spatial resolution is not as high as CT or MRI. One of the goals of the portfolio is to develop a new generation of tools that matches or betters the spatial resolution of CT/MRI while retaining the portability and higher durability of ultrasound devices.

The demand for a solution including a portable tool that can offer high-resolution images of soft tissue and bone is quite high in both the military and domestic markets. One potential strategy is to use visible, infrared, or terahertz radiation to obtain images of physiological structures. TATRC has sponsored a number of projects in this area as photons in these energy ranges may provide high resolution data of dermal injuries while maintaining overall portability.

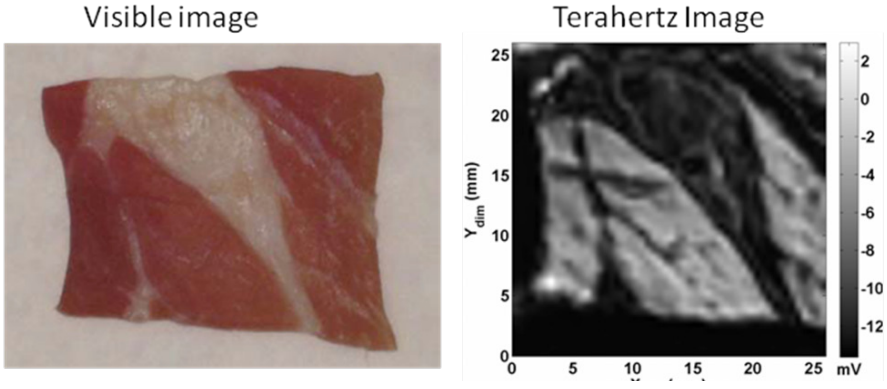
Dr. Greg Mooradian is working with TATRC on a hyperspectral imaging tool that not only detects cancer, but also links the technology to treatment using photodynamic therapy. Dr. Mooradian's technology is based on a technique called hyperspectral imaging, which permits sub-dermal image retrieval. The images can be used to plan treatment dosimetry for the treatment light source.

Terahertz imaging

Terahertz (THz) radiation is defined as the submillimeter (1 mm - 0.1 mm) electromagnetic spectrum with frequencies between 300 Gigahertz (GHz) and 3 THz, and is a relatively new and expanding area that promises unique imaging capability. Due to the high absorption of THz electromagnetic radiation in water, reflective THz imaging has distinct advantages over earlier transmission-based systems.

Furthermore the high dielectric constant of water at these frequencies lends itself well to the detection of slight variations in water content of biological materials.

A reflective THz imaging system is being developed in collaboration with the Brown Research Group at University of California, Santa Barbara (USCB). These groups are seeking to determine the viability of reflective THz imaging to various medical applications, while improving the prototype system's already high signal-to-noise ratio, sensitivity, and spatial resolution. Preliminary results have already been obtained on various soft tissues, and more applications are currently under extensive study.



A comparison of visible and THz images of prosciutto ham sample using THz imaging system after upgrade.

Other potential uses include monitoring burns and determining the degree of damage, the detection and monitoring the formation heterotopic ossifications and the detection and monitoring of ocular trauma and disease. TATRC is in the midst of setting up strategic partnerships for each of these relevant issues.

Imaging Agents

Visualization of disease or physiological insult on the molecular or cellular levels is a continued research emphasis in the health care industry. One strategy to attain this level of resolution is to use contrast agents to bolster the strengths of conventional imaging techniques such as ultrasound or MRI. Other techniques such as positron emission tomography (PET) are entirely dependent upon innovations in small molecule development to achieve region-of-interest contrast over native or benign structures.

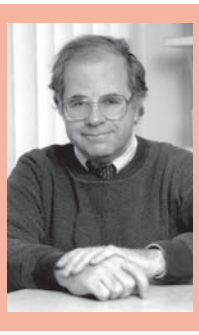
While research in this area has been robust for each of the imaging modalities described previously, there are several easily identifiable areas for improvement. For example, while contrast-enhanced MRI imaging using Gadolinium-based agents have seen a good deal of utility across a variety of clinical applications, they are somewhat limited by their toxicity. This becomes increasingly important with an injured Warfighter. Other agents such as superparamagnetic iron oxides (SPIOs) show promise, but their mechanism of action with respect to some applications, such as neuroimaging, is not completely understood. Newer compounds are needed that will not only address these concerns but also boost the current levels of sensitivity and specificity for these agents.

PET imaging offers some genuine advantages over contrast agents due to the high specificity of the imaging agents used. Unfortunately, the rational design of new agents is quite challenging from biochemical and synthetic perspectives. As a consequence, there are fewer than a dozen targets that PET focuses on for brain injuries.

These are just a few examples that are intended to highlight the need for new, multidisciplinary research endeavors in this area. The next generation of research needs to go beyond the basic scope of examining pharmacodynamics and new applica-

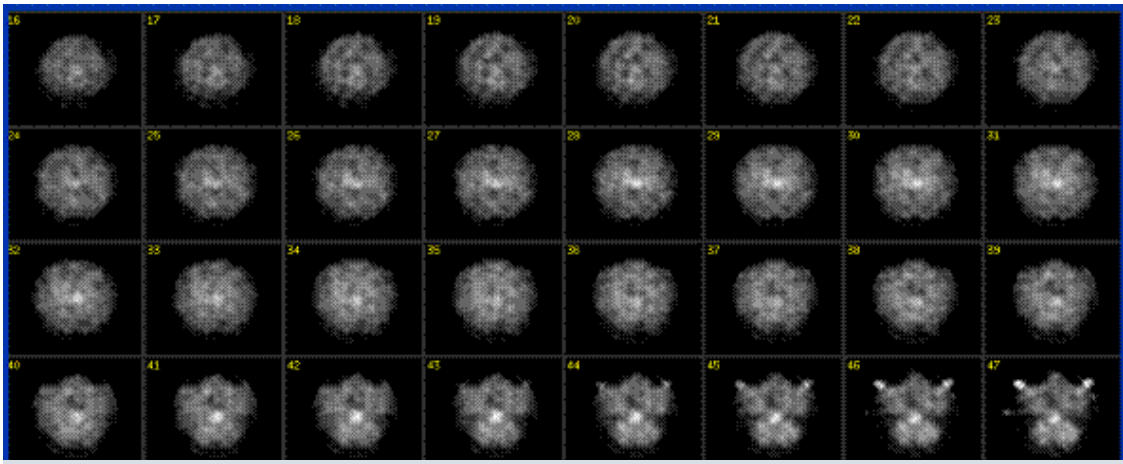
"The potential of imaging to teach us about in vivo brain neurochemistry offers both promise and challenge."

Dr. Kenneth Marek
Institute for Neurodegenerative Disorders



tions of existing molecules and more towards the development of new molecular architectures that will enhance both sensitivity and specificity for newly identified targets.

To answer this challenge, both Caldera Pharmaceuticals and the Institute for Neurodegenerative Disorders have partnered with TATRC to develop the next generation of agents MRI and PET imaging.



An example of single photon emission tomography (SPECT) of a PD subject after injection of [I-123] CLINDE showing uptake in striatum and midbrain regions.

Dr. Eva Birnbaum and her team at Caldera are developing alternatives to Gadolinium-based contrast agents. Drawing upon conventions supported by earlier contrast agent research, Dr. Birnbaum is investigating other elements such Dysprosium as an alternative to Gadolinium. Dysprosium may reduce the dose needed for contrast enhancement as compared to Gadolinium. Secondly, Dr. Birnbaum's research supports investigations which may boost the specificity to enhance regions of interest.

Dr. Ken Marek of the Institute for Neurodegenerative Disorders continues to focus on innovations in clinical care and medicinal chemistry. As a clinician, Dr. Marek leads some of the country's largest Alzheimer's disease and Parkinsonism disease imaging studies and is constantly on the search for new PET diagnostic agents. Dr. Marek has recently focused on the validation of a new imaging agent for neuroinflammation named CLINDE, which may be a marker for the progression of either disease. Dr. Marek is currently conducting a clinical trial to test this hypothesis. In addition to our aging community, this research has become increasingly important as many symptoms of these diseases are manifesting themselves in brain-injured service members.

Data Visualization

Data Visualization is related to the complexities of using multiple image modalities to gain a "full picture" of disease or injury. Most modern radiology facilities are quite capable registering multiple modalities to develop a complete picture of the damage or disease, but unfortunately the process is quite tedious and varies from institution to institution. While great strides are being made to develop image registration standards, the concept of developing a full featured image visualization station remains elusive. Developing such a solution will save time and perhaps provide new insights on how to stream the image registration process for enhanced detection and diagnosis.

Dr. Harvey Neiman of the American College of Radiology (ACR) has developed an imaging platform capable of integrating radiological standards and technology to produce composite images of human physiology spanning several imaging techniques. The platform supports the testing and validation of new image registration strategies to:

- Catalyze the development of the "next generation" of image visualization for injuries and disease; and
- Greatly reduce the costs of, and increase the uniformity of, advanced imaging software deployed across military and civilian clinics.

Thus far, this project is being tested for use with TBI datasets that require complex data visualization routines. Preliminary data has shown that the platform is an efficient tool for visualizing DTI data. The current focus is on the military healthcare system, but the tool has the potential to translate into the domestic setting as well.

International Health

Supporting US Africa Command (AFRICOM) and other COCOMS

Emerging DoD priorities in the international setting now call for an emphasis on civil-military cooperation and medical stability operations. Accordingly, TATRC's international health mission is focused on defining how technologies can be designed and/or adapted and then applied and sustained across a broad spectrum of US military missions overseas.

Congolese child suffering from monkeypox a potentially fatal disease in children.

Technologies That Enable Remote Data Collection

Digital Pen Technology Demonstration- Field Use In Remote Overseas Clinical Study

A monkeypox clinical observational study is being conducted by the US Army Medical Research Institute of Infectious Diseases (USAMRIID) in the Democratic Republic of the Congo (DRC), the only region of the world where human disease occurs with high rates of endemicity. The study involves obtaining clinical history, vital signs, physical exam findings and laboratory data from hospitalized monkeypox patients to better understand the nature and extent of disease. This will provide human data about orthopoxvirus infections to support investigational new drug development and FDA approval.

The remote study site has only a satellite phone and internet connection with the outside world. All personnel, supplies and equipment must be flown by chartered aircraft into to this remote rural jungle hospital facility from Kinshasa, which is 800 miles away. The study data are collected manually by Congolese collaborators.

Study investigators would like to utilize technology to collect, share, document, and transmit study data from the field site back to Fort Detrick, MD for oversight, monitoring, and analysis. This type of capability would greatly enhance data collection methods, automate the information importing process, and improve efficiency of the study.

The digital pen technology—a smart pen which is a pen/computer hybrid—from ADAPX has been identified as a candidate technology to address the needs of researchers.

The pens write in ink and contain infrared readers that track vectors made on pre-printed stationery which has specifically unique patterns of nearly microscopic dots and store the information until it is uploaded to a computer. Once the pen is docked,

Portfolio Team

Cynthia Barrigan

Far Left: The digital pen data collection tool, housed in its USB recharging holster, which also allows for data upload a configured laptop.

Left: As part of study specific training a Congolese nurse uses the digital pen.

Right: Dr. James Martin, principal investigator, and Dr. Therese Rui, the hospital director, demonstrate that the image uploaded to a laptop computer is identical to the handwritten signatures recorded in the log book.

the information is loaded into specific software which can be manipulated to populate data fields as well as recreate and save the recorded Case Report Form (CRF) image. The original case report form (which was completed by hand using the digital pen—simultaneously functioning as an ink pen) potentially becomes the source document for the study and serves as a back up to the digital data collection.

A demonstration is currently underway and results will be available in the summer of 2010. TATRC will carefully review outcomes to help inform future technology research and development in the area of remote data collection.

Use Of Cell Phones For Electronic Disease Surveillance In Low-Resource Settings

Disease surveillance, "is the cornerstone of public health security," according to the World Health Organization. In many developing countries, human, laboratory and infrastructure limitations impede effective surveillance. To enhance situational awareness and foster public health data sharing in the area of disease surveillance, the Armed Forces Health Surveillance Center (AFHSC), DoD Global Emerging Infections Surveillance and Response System (GEIS) is currently providing HIT outreach to aid the Peruvian military in expanding access to communication networks and technology to support disease surveillance.

AFHSC/GEIS in partnership with the US Laboratory in Lima, Peru, the Naval Medical Research Center Detachment (NMRC-D), and the US Southern Command (USSOUTHCOM) have implemented a commercial electronic disease surveillance system called Alerta for use by the Peruvian military. This initiative continues to evolve with recent GEIS investments now targeted at the development of an alternative platform that uses open source software tools instead of proprietary software systems. The goal is to offer developing countries options for creating affordable and sustainable solutions that meet their needs.

To design opens source solutions, GEIS has partnered with the Johns Hopkins University Applied Physics Laboratory (JHU APL). They are currently building a comprehensive suite of open-source tools that facilitate data collection, analysis and reporting.

Recently, TATRC has partnered with GEIS/JHU APL to lend its support for the development of cell phone-based applications for the capture and transmission of data by healthcare providers working in remote areas. These applications will be added to the overall suite of tools made available by GEIS.

Testing and evaluation will continue in Peru in FY10. The lessons learned and eventual system adopted by Peruvian military will be offered to neighboring countries and other regions of the world—such as Africa and Asia—as a model. It is envisioned that further adaptation of these tools will occur moving forward.

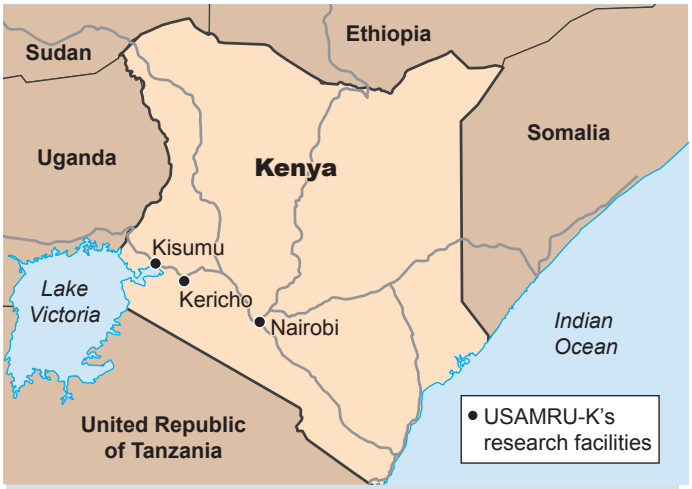
Strengthening Austere Medical Networks

US Army Medical Research Unit-Kenya (USAMRU-K): Telecommunication Network Enhancements

The US Army Medical Research Unit - Kenya (USAMRU-K) is one of five US military overseas research laboratories. It was established in 1969 at the invitation of the Kenyan Government to study trypanosomiasis in Western Kenya. It was later permanently established in 1973 and its scope of research expanded.

USAMRU-K is headquartered in Nairobi, Kenya with two main satellite laboratories in Kericho and Kisumu. The lab works through cooperative agreements with Kenya Medical Research Institute and the Henry Jackson Foundation. The USAMRU-K Mission is to:

- Develop and test improved means for predicting, detecting, preventing, and treating infectious disease threats important to the US military and the host nation;
- Conduct surveillance, training, research, and response activities related to emerging infectious disease threats;
- Partner in executing the President's Emergency Plan for AIDS Relief and the President's Malaria Initiative; and
- Support the AFRICOM Commander's health related Theater Security Cooperation objectives through engagement of nations in the region.



The geographic location of USAMRU-K's three research facilities in Kisumu, Kericho. and Nairobi.

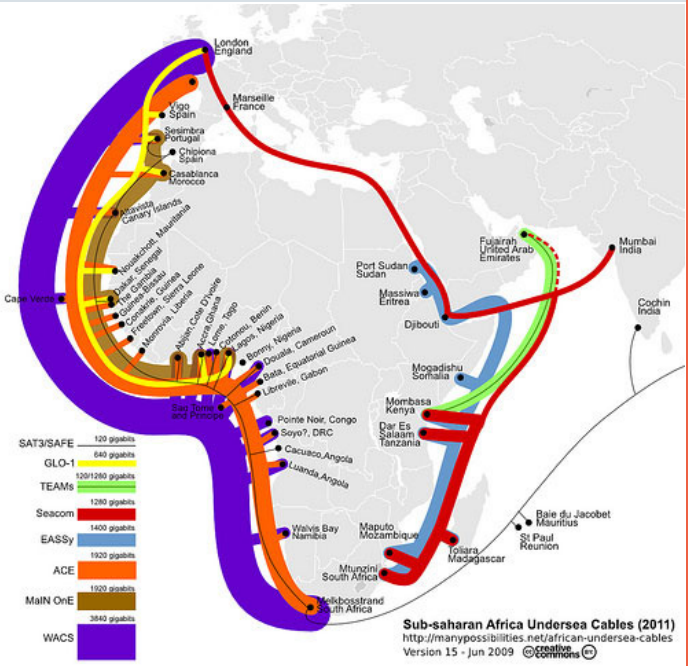
USAMRU-K faces many challenges. Its research facilities are located 170 miles from the main facility across rugged terrain. Due to a lack of technical infrastructure, communications are slow and disjointed. The most critical infrastructure issues are the lack of bandwidth and absence of network interoperability between the research sites.

Currently, each research site is served by a satellite dish with a direct link to Europe. The available bandwidth is grossly inadequate to handle even normal e-mail traffic and existing satellite bandwidth is expensive.

The plan for this project is to improve the quality of existing USAMRU-K networks by harnessing the newly arrived undersea fiber optic technology and adding hardware in support of a more robust LAN, data storage capability and C4I management.

Once completed in early 2010, all three research facilities located across Kenya (Nairobi, Kisumu and Kericho) will be connected to the main fiber optic cable backbone and networked to each other for improved communications.

The 10,500-mile cable, built by SEACOM, a consortium 75% controlled by African investors, became operational in Kenya on July 23, cost $650 million, and links Eastern and Southern Africa with Europe and Asia. Within the next year two more submarine fiber systems are expected to be added in East Africa.



Mobile Learning (mLearning) Systems For Medical Personnel Readiness

Medical Stability Operations (MSO) Training Summit

To meet today's mission, DoD health care personnel require specialized training that prepares them for capacity-building efforts in peace, conflict, and post-conflict environments in coordination with other US government agencies and host country governments.

A better understanding of military medical diplomacy concepts and increased awareness of roles, responsibilities and cultural differences of a wide range of contributing partners can help improve mission outcomes, save resources and provide a smoother hand-off during transition.

In a first of its kind effort to introduce new training tools in Medical Stability Operations (MSO), the Defense Medical Readiness Training Institute (DMRTI), in partnership with Force Health Protection & Readiness (FHP&R), International Health Division (IHD) and TATRC, hosted an interagency MSO Training Summit to identify and bridge education gaps in approaches to global health capacity building missions conducted by DoD and the US government as a whole.

To devise the best approach, DMRTI invited experts from across all military Services, Combatant Commands and Interagency partners to discuss MSO concepts and collectively think about course design. A major focus of the meeting was placed on the definition of training objectives and the review of course topics. Various partners presented candidate course materiel to the audience for consideration.

In addition to a focus on content, an emphasis is being placed on leveraging the latest in training technologies. Given the fast pace of deployments, it is imperative that the course be made available through a variety of distributed learning systems—including mLearning platforms such as smartphones. TATRC serves as the Technical Consultant to DMRTI and will be facilitating the development of a mobile learning environment for the MSO course.

Smartphones, such as these, are a vital platform for m-learning.

Health IT Outreach- Building Partner Capacity Through Enhanced Health Sector Collaboration

1st Annual AFRICOM Component Surgeons Conference

With TATRC support, the AFRICOM Surgeon convened the first conference of Component Surgeons in Germany, in August 2009.

Planned during the initial year of stand-up for AFRICOM, this seminal event was important in establishing a cohesive medical leadership for the region and working towards a unified vision for health engagements on the continent of Africa.

Important themes covered at the meeting included: challenges of working on the African continent; Force Health Protection issues, such as aeromedical evacuations; emerging health technologies, including mobile telecommunications; and legal authorities required for operations in the region.

A special emphasis was placed on establishing partnerships in the areas of medical research, technology, and training and logistics to ensure Component Surgeons are best prepared to meet their respective

missions, as well as work on developing a collective capacity to address priority health issues.

In addition to providing a foundation for medical leadership in Africa, the conference succeeded in establishing a framework for informing and educating the AFRICOM and its Component staff and partners in the latest health technology science and applications that could be useful for application in the Africa Command Area of Responsibility (AOR).

SOUTHCOM Health ICT Interagency and Component Surgeons Conference

The SOUTHCOM has a growing interest in leveraging health information and communications technology (Health ICT) to attain greater impact and more enduring outcomes in its health sector programs and activities in Latin America and the Caribbean.

In September 2009, for the first time, the US SOUTHCOM Surgeons Office convened the US health sector community from across the region to harmonize and synchronize efforts, programs, resources and information. The intent was to establish a working baseline, and from there, explore opportunities for mutually applying Health ICT applications in a way that enhances regional stability and security and enables expanded partnerships.

The goal of the meeting was to begin to identify practical Health ICT solutions and a way ahead on how a range of services at the "technological edge"

Organizations Represented: US Army Command Surgeon and Component Surgeons (USARAF; NAVAF; AFAFRICA; CJTF-HOA; SOCAF) USAID; WRAIR; TATRC; HEALTH AFFAIRS;CHPPMEUR; USAMMCE; BUMED; DIMO; DMRTI; USUHS/CDHAM.

of population health and clinical medicine can be used and applied to further health related objectives in the AOR.

Eighty senior subject-matter experts from US organizations involved in the planning, funding, support, execution, and evaluation of US sponsored health sector activities in US SOUTHCOM AOR attended.

Participating agencies obtained an unprecedented perspective on the depth and breadth of US Government sponsored health sector activities happening in the region and identified current and new potential applications for Health ICT in the AOR.

Represented Organizations: HQ US SOUTHCOM, JFCOM, CENTCOM, USARSO, AFSOUTH, NAVSO, SOCSO, JTF-B; JIATF-SOUTH, OASD/Health Affairs, OASD/ Network Integration, US Navy's Fleet Forces Command, TATRC, NMRD-Peru, WRAIR, CDHAM, WRAMC, DoD GEIS, ANG SPP, Civil Affairs Units, USUHS, DHS, DHHS, CDC, USAID, OFDA, University of Miami, University of Texas. Component Surgeons, USAID, and CDC.

Third Intensive Balkan Telemedicine & E-Health Seminar

A series of meetings were planned to assist partners in the Balkan Region build capacity to design and implement national and regional telemedicine systems in Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Greece, Kosova, Macedonia, Montenegro, and Serbia.

In February, the International Virtual e-Hospital Foundation (IVeH), in collaboration with the Ministry of Health of Macedonia, held a two-day intensive telemedicine and e-health seminar in Skopje, Macedonia. TATRC co-chaired the event.

This workshop was part of the ongoing scheduled activities for the IVeH implementing a two-year project "Improving Health Care in the Balkans Using Telemedicine, Advanced Technologies and Cultural Exchange Program as a Platform," funded by the Bureau of Education and Cultural Affairs of the US Department of State.

Over 200 attendees from government, academia, the military, US Department of State and the US Agency for International Development (USAID) came from across the region—including participants from the Bondsteel US Army Base in Kosova.

As with the previous two seminars, clinical applications and evidence-based outcomes of telemedicine and e-health technology as it pertains to current technologies, principles, practices and applications of telemedicine and e-health were discussed.

The previous two Balkan intensive telemedicine seminars have resulted in the creation of the country-wide and now renowned telemedicine program in the Republic of Kosova (www.telemedks.org) and initiation of the implementation of an integrated telemedicine and e-health program in Albania.

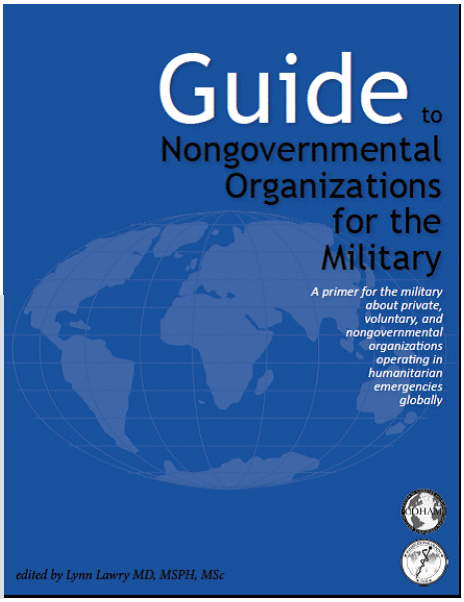
This Third Seminar served as the catalyst for the adoption of telemedicine in Macedonia as part of the larger regional initiative.

Guide to Nongovernmental Organizations for the Military

The Center for Disaster and Humanitarian Assistance Medicine (CDHAM) in partnership with many experts has published a new edition of the "Guide to Nongovernmental Organizations for the Military."

The Guide is intended to serve as a resource for deployed US military personnel or others involved in the planning and coordination of international health engagements. The book aims to bring about a heightened awareness of the nongovernmental organizations (NGO) sector and provide important contextual information that will aid military personnel in setting expectations and facilitating interactions with NGOs when operating in a common environment.

One chapter, authored by TATRC, focuses on how NGOs use health ICT to collect and exchange information and communicate during a humanitarian crisis. TATRC has developed expertise in this area as part of its international HIT outreach efforts. A key component of those outreach efforts includes exploring opportunities for dual-use technology transfer to other sectors.



This publication was funded and published by the Center for Disaster and Humanitarian Assistance Medicine. CDHAM is a university-based venture within the Department of Military and Emergency Medicine (MEM) at the Uniformed Services University of Health Sciences (USUHS).

Infectious Disease

www.tatrc.org/infectiousdisease

Novel Antibacterial Technology for Wound Infections

Many battlefield-related wound infections today are extremely difficult to treat because bacterial pathogens are rapidly developing resistance to all currently used antibiotics. This leads to extended hospitalization, increased risk of amputation and sometimes death. These pathogens are becoming a major problem in civilian hospitals as well.

ConjuGon, Inc., is developing a new technology to eliminate infections caused by antibiotic-resistant, Gram-negative bacteria. It works in a completely different way, such that drug resistance is no longer an issue.

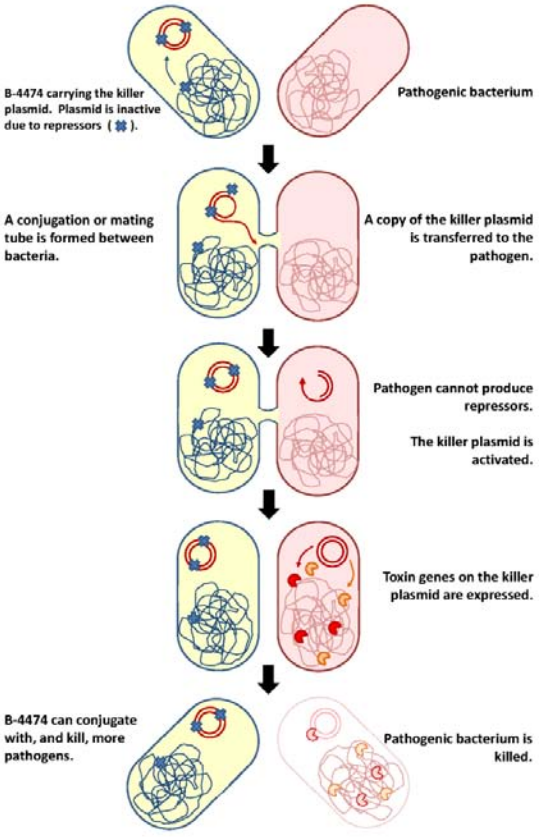
ConjuGon's technology is based on conjugation, a natural process by which DNA is transferred from a donor bacterium to a recipient bacterium. ConjuGon uses conjugation to introduce genes into pathogens that, when expressed, will kill those pathogens with extremely high efficiency. The donor bacterium has been engineered to minimize human toxicity, to be unable to replicate in the environment or in the body, and to maintain and protect itself from the killer plasmid.

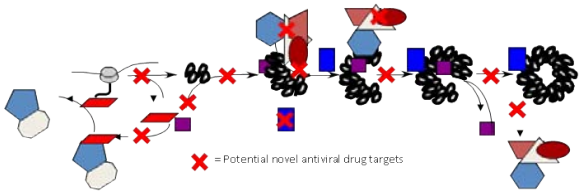
"With TATRC support, we are finalizing a marketable product and beginning the process of testing required for FDA approval so we can get this therapy out to the Warfighter." says Dr. Steven Watt, principal investigator.

Defense Against Viral Illness

The military faces a pressing need for antiviral drugs to protect Warfighters from an array of viruses. Most drug development has focused on targeting a specific virus—which means there will be a lag between the emergence of a new strain and the production of a drug to fight it. However, Dr. Vishwanath Lingappa and his group at University of California San Francisco discovered that viruses use the host animal's or person's proteins to assemble structures called capsids, which are needed for a virus to reproduce.

TATRC is supporting researchers at CUBRC, Inc., and Prosetta Bioconformatics Corporation who are identifying host factors that will inhibit





ConjuGon's novel therapeutic kills many bacteria, including those that are resistant to conventional antibiotics. The technology was presented at a MIDRP wound conference, as well as the TATRC Product Line Review.

Portfolio Team

Amber Stanley
Dr. John Carney
Jami Durrschmidt

influenza virus capsid assembly. The work builds upon Lingappa's and Program Manager Dr. Anne Radcliff's other applications of this technology to public health threats such as HIV and highly lethal infectious diseases of importance in biodefense.

"This line of discovery research shows great promise. Because the approach targets the host, not the virus, the normal mechanism by which viruses mutate to develop drug resistance is much less effective. Plus, the host is protected against multiple viruses because they won't have a basic protein needed to produce infectious virus particles. This could be the beginning of a whole new class of antiviral compounds." says Radcliff.

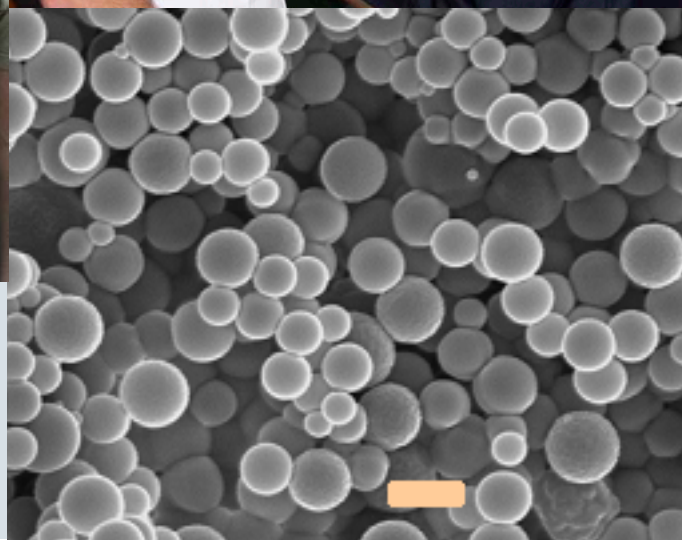
Microencapsulation and Vaccine Delivery

More effective and easily stored vaccines are a critical tool in the military's defense against possible viral warfare or terrorist attacks. Investigators at Texas A&M University are engaged in promising research in microencapsulation of vaccines, entrapping them within micro- or nano-particles, as a way to enhance their effectiveness. These encapsulated vaccines could have the capability to be shipped at room temperature and taken orally in a single dose.

TATRC is supporting the group's efforts to develop prototype controlled release vaccines and take them into animal testing, with the goal of improving the delivery of a number of vital vaccines.

"Controlled release could potentially reduce the amount of antigen needed, protect the antigen for storage and target it to specific tissues. We are exploring particles that enable oral or intranasal delivery without side effects." states Dr. Allison Ficht, the project's Principal investigator.

CAPT Mark Beavers discusses a project with a PI.



Investigators of Texas A&M University are working on a new, more effective vaccine delivery method. Shown are microcapsules produced through emulsion technology; they allow for controlled release of a vaccine.

Human Performance Optimization

Human performance optimization (HPO) and enhancement (HPE) science and technology is a longstanding Army niche in medical research. In this area, TATRC explores new opportunities and directly supports the US lead medical performance research lab, USARIEM, and the Military Operational Medicine Research Program (MOMRP). Performance can be optimized through the way we feed, train, rest, lead, and treat individuals and teams; technology advances such as functional imaging, virtual environments, biomonitoring systems provide opportunities to improve the scientific basis of these "prescriptions" for optimal performance and the understanding of interventions that may enhance physical and mental performance aspects. Important near-term priorities for the military are to: enhance physical training while reducing musculoskeletal injury rates; improve weight management and fitness maintenance; and increase mental and physical resilience for benefits ranging from reduced susceptibility to infectious disease and chemical toxicity to improved wellness, endurance, and work capacity.

Right: Research participant performs isokinetic torso strength test at the Human Performance Research Laboratory.

Below: Research participants perform agility component of ETAP at the Human Performance Research Center.

These are young men and women in top physical condition. This population is going to do more than get up and walk to the TV to change the channel. They're going to try and win gold medals. So we need to learn how to help them do that."

LTC Rachel Evans, PT, PhD
Research Directior, National Center for the Intrepid.

Portfolio Team

Dr. Sylvain Cardin
LTC Teresa Brininger
Ashley Fisher
Greg Wimsatt

"The effects of the data from the University of Pittsburgh research have been immediate and profound … implementation in the next phase of the project will yield long-term positive results that will enhance the medical readiness and combat effectiveness of all Soldiers."

MG Jeffrey Schloesser, US Army Commanding General 101st Airborn Air Assault Division, Fort Campbell, KY

Injury Prevention and Performance Optimization in Warfighters of the Army 101st Airborne/Air Assault Division

One of the leading projects in this portfolio is a cooperative project between TATRC, University of Pittsburgh, and the 101st Airborne Division at Fort Campbell, KY. The fundamental concept is to treat Warfighters as elite "tactical" athletes with a fitness program tailored to their needs. This multi-phase research initiative is creating a systematic, data driven, and sustainable injury prevention and performance optimization training program to reduce the risk of unintentional, musculoskeletal injuries and enhance military readiness in 101st Airborne/ Air Assault Warfighters. The early successes of this effort have led to a second test site with the Navy Special Operations unit in Little Creek, VA.

This project assesses biomechanical, musculoskeletal, physiological, and nutritional interventions for Warfighters of the Army 101st Airborne/Air Assault in order to improve safety and performance of the individual Warfighter, along with weight management, with goals of reducing chronic disease risk, extending their time on active duty, and enhance the quality of life after the military. An optimizing program will ultimately decrease the time lost due to disability, reduce personnel attrition, and reduce the financial burden associated with medical expenses and disability payments.

This project is executed through an on-site 101st Airborne/Air Assault Human Performance research laboratory in collaboration with the University of Pittsburgh Neuromuscular Research Laboratory. In addition to the development and evaluation of an 8-week training program, the Evaluation Technical Assistance Project (ETAP), related goals are being implemented through development and presentation of a nutritional education seminar series and outreach materials; development of a military performance and epidemiology database from which specific injury and performance related queries may be processed; data collection at the 101st Airborne/Air Assault Human Performance Research Laboratory, and development of new technologies to identify risk factors for unintentional musculoskeletal injury.

Developing a Brief Method for the Simultaneous Assessment of Anaerobic and Aerobic Fitness/Gait Dynamics and Locomotor Metabolism

This project is executed in collaboration with Southern Methodist University. Metabolic energy expenditure, thermoregulation and aerobic fitness are relevant to Warfighters in the field and to the civilian population in day to day life. The metabolic energy expended during locomotion on a chronic basis could be used to provide feedback to assure

Military rations "then and now." Left: Soldiers at mealtime during the Civil War. Above: A Soldier samples new rations. (Photo by Andricka Thomas US Army)

that levels of physical activity meet desirable target levels. Accordingly, work in this area has the potential to provide the global health benefits conferred by adequate amounts of regular weight-bearing exercise. These include the maintenance and promotion of cardiovascular fitness and health, bone density, desirable body composition, and the avoidance of obesity, Type 2 diabetes, and other metabolic disorders. This work is developing accurate, field-expedient techniques for assessing aerobic fitness from rates of energy expenditure during walking using weight and height.

Troop Recruitment Improvement (TRIM)

The long-term goal of Troop Recruitment Improvement (TRIM) is to provide definitive information on the factors that underlie the development of obesity in young persons. This knowledge will help insure the availability of a large pool of youth who are fit and ready for military service. This project is a multi-center observational investigation conducted by South Carolina Research Authority, University of South Carolina (including South Carolina State University), Clemson University, Medical University of South Carolina, The Cooper Institute, Pennington Biomedical Research Center (PBRC), University of Iowa. The proposed TRIM design is using state-of-the-art measures to characterize the range of factors influencing overweight in children and adolescents from early childhood to recruitment age in a comprehensive and coordinated manner. This phase of the project (TRIM II) is to pilot test those measures and methods.

Bone Health and Military Medical Readiness

LTC (Dr.) Dani Moran (Sheba Medical Center, Israel) performed detailed analyses of the data from the US-Israeli military stress fracture studies examining biochemical and bone property biomarkers of injury risk during recruit training. This collaboration between the Israeli Defence Forces and USARIEM is investigating novel approaches to characterizing injury susceptibility and exploring the use of peripheral Quantitative Computed Tomography (pQCT) technology for tibial bone scans. A new effort was initiated in modeling this and other data to develop more accurate physical training planning tools that will predict injury risks for individuals and teams. TATRC also joined other federal agencies to co-sponsor a reassessment of national recommendations Vitamin D and calcium Dietary Reference Intakes by the Institute of Medicine. The military interests extend to standardization of methods to assess Vitamin D status in recruits, safe upper limits of supplementation of Vitamin D and calcium to reduce the rate of stress fracture in recruits, and evaluation of other health and performance benefits attributed to doses of Vitamin D higher than the levels traditionally associated with bone health.

New efforts are being initiated in modeling data to develop more accurate physical training planning tools that will predict bone injury risks.

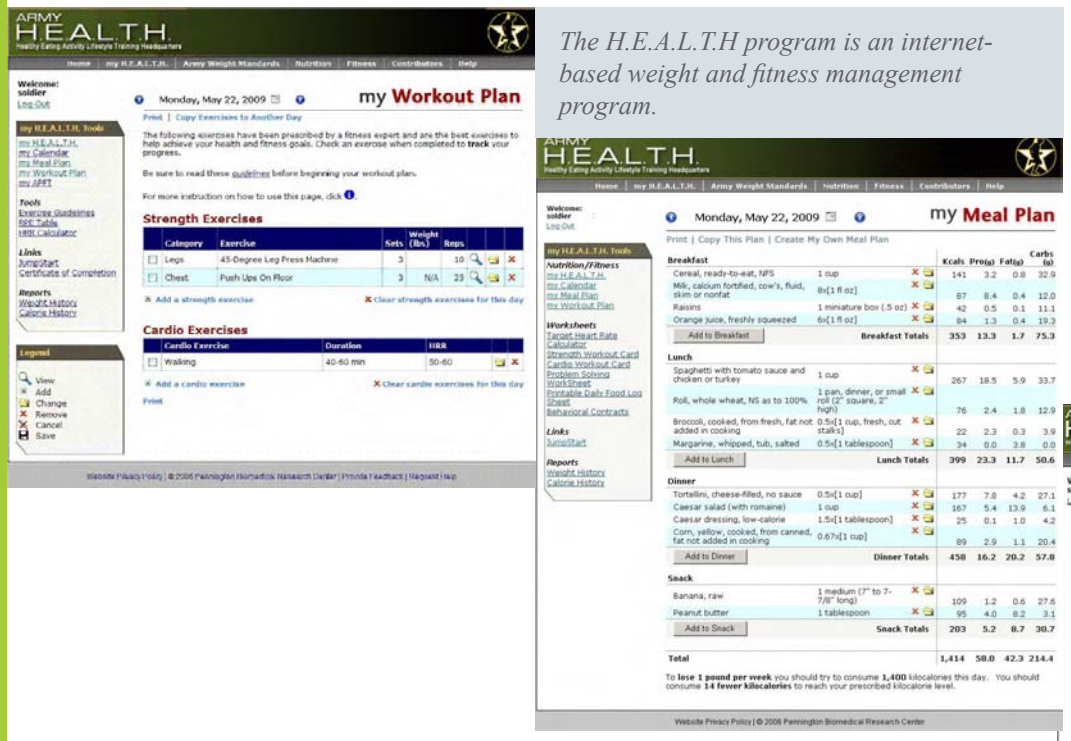
Personnel Readiness and Warfighter Performance

Since 1989, the Pennington Biomedical Research Center (PBRC), in Baton Rouge, LA, has collaborated on 92 major military nutrition projects and field studies and coauthored over 100 technical papers with military researchers. PBRC continues to provide substantial collaboration, expert consultation, and technical support to the military nutrition and performance research programs at the USARIEM and in support of key objectives of the MOMRP. In 2009, PBRC collaborated on five core projects with USARIEM:

- The effect of amino acid supplementation on skeletal muscle protein turnover following endurance exercise;
- Gender difference in energy balance regulation;

- Effect of varying altitudes on acute mountain sickness, and physical and cognitive work performances in the unacclimatized Warfighter;
- Effect of tyrosine supplementation on cognitive performance and mood during military stress; and
- Effects of meal duration on biological markers of hunger and satiety.

An ambitious longitudinal study on weight management and fitness in Army Reserve forces was launched after several years of preliminary development and planning. This study uses a computer-based data collection system for tracking body weight/body fat and fitness in Warfighters, and an internet-based weight and fitness management program, the Healthy Eating, Activity, Lifestyle Training Headquarters (H.E.A.L.T.H.) previously pioneered by PBRC and USARIEM at Fort Bragg. Another study piloted these tools over three years with the 94th Regional Readiness Command (RRC) monitoring fatness and physical performance of reservists for two years after a one-year baseline period. The new study, a randomized controlled trial, is designed to test the efficacy of the H.E.A.L.T.H. intervention for prevention of weight gain, reducing fatness, and increasing fitness as measured by the Army Physical Fitness Test (APFT). This intervention study is being conducted with the Louisiana Army National Guard. A related effort by this team led by Dr. Williamson developed a digital photography method for measuring food intake and food selections; this is continuing with development and validation of a semi-automated method for quantifying data derived from digital photography.



The H.E.A.L.T.H program is an internet-based weight and fitness management program.

Psychological Health/ Resilience & Reintegration

Since the beginning of Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF), Warfighters' psychological health, and strategies to build resilience, retrain and reset Warriors have remained a high priority. The Psychological Health and Resilience and Reintegration portfolios focus on a wide range of relevant military issues related to mental and physical health that include TBI, PTSD, and Warriors in transition. Although individual projects often span a number of TATRC portfolios such as Modeling and Simulation, Imaging, Integrative Medicine, and Wellness and Training, the Psychological Health and Resilience and Reintegration portfolios focus on studies examining the physical and mental health impact and consequences of military personnel and aim to improve the functioning and well being of Service Members. The Psychological Health portfolio gives special attention to the underlying causes, risk factors, consequences, symptoms and treatments of psychological trauma. The Resilience and Reintegration portfolio focuses on studies investigating all aspects of physical and mental rehabilitation, resilience and reintegration into the community or return to duty. Across both portfolios, studies range from "bench to battlefield," exploring a variety of biological mechanisms to innovative remote deployments of physical and psychological treatments in austere environments.

Examples of specific aims targeted by recent investigations associated with these portfolios include:

- Developing a more clear understanding of the long-term effects of the consequences and potential long-term impacts of physical and psychological trauma.
- Examining innovative use of technology to create new models for psychological and rehabilitative treatments.
- Exploring care delivery models for providing psychological and reintegration services to Veterans and their families who live in rural areas.
- Further exploring and developing automated neurocognitive testing to identify and monitor changes in cognitive function in Service Members.
- Improving the quality of life for Service Members by developing and implementing innovative assistive technologies.

Specific examples are cited below.

Relationship Between PTSD and Risk of Dementia

Understanding the consequences and potential long-term impacts of psychological trauma is critical in developing and advocating for early intervention to prevent long term mental health problems among service members. The NCIRE is affiliated with the SFVAMC and the UCSF and funds reviewed projects on important DoD medical problems. A NCIRE sponsored project led by Dr. Kristine Yaffe provided evidence of a relationship between PTSD and dementia. Researchers retrospectively com-

Psychological Health/ Resilience & Reintegration

Portfolio Teams

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Resilience & Reintegration
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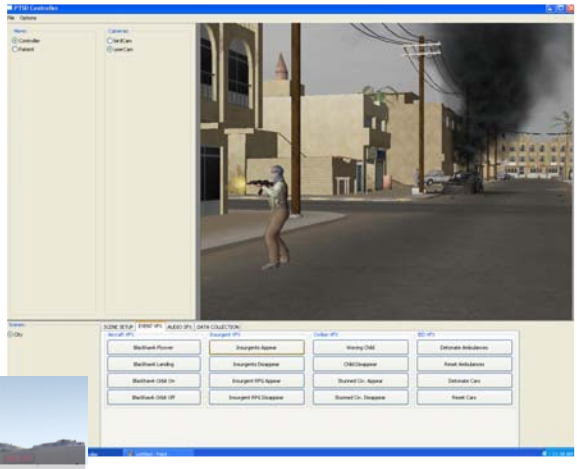
Philip Zakas

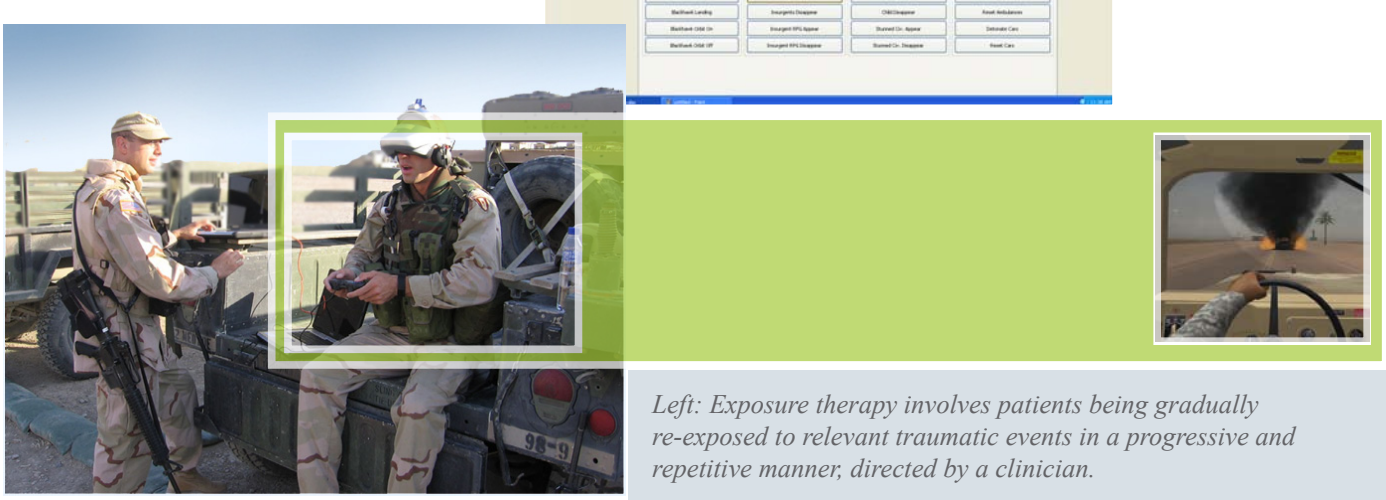
pared patients who had been diagnosed with PTSD to those who had not been diagnosed. Dr. Yaffe reported that Veterans with PTSD had an 11% rate of dementia compared to a 7% rate for those without PTSD. Patients with PTSD had a 2.3 times greater risk of developing dementia and a 1.77 times greater risk when adjusting for other health problems (e.g., depression, substance abuse). Although further investigation is required to understand the underlying mechanism, these findings speak to the importance of screening patients with PTSD for cognitive problems and identifying and treating PTSD symptoms early as a possible way to mitigate cognitive problems down the road.

Virtual Therapies for Psychological Trauma: Virtual Iraq

The rapidly growing field of Clinical Virtual Reality holds promise for innovative treatments for PTSD. Exposure therapy is a well researched, evidence-based treatment for PTSD that involves patients being gradually re-exposed to relevant traumatic events in a progressive and repetitive manner, directed by a clinician. This often involves re-imagining the trauma through guided visualizations with a therapist. Exposure therapy helps to slowly desensitize the patient to the strong emotional and physiological responses triggered by memories of traumatic events and helps the patient to process these memories in an effort to increase adaptive coping. Using virtual reality exposure may enhance treatment by providing a more controlled method for prompting this re-imagining and may circumvent the patients' natural (albeit counterproductive) tendencies to avoid painful memories during treatment sessions.

TATRC's Simulation and Modeling portfolio in partnership with the Office of Naval Research (ONR), The US Army Research, Development, and Engineering Command, DCoE, and the USAF has been supporting work on virtual reality by Dr. Skip Rizzo from the University of Southern California's Institute of Creative Technologies (ICT) along with his national colleagues and collaborators. This project developed a series of virtual Iraq environments to be used for exposure therapy with Iraq combat Veterans with PTSD. The virtual environment was initially designed from an X-Box® game and US Army funded combat simulation trainer. Virtual Iraq consists of multiple combat environments (city and desert road) that were created to simulate common combat experiences in Iraq including Humvee patrols, IEDs, and ground combat. Patients can use either a game controller or replica M4 to navigate the game environment. The virtual reality component uses a VR helmet, 3D audio, and vibrotactile and olfactory stimuli with physiological monitoring. The therapist is able to modify and change the experience in real time. The treatment consists of 2 weekly, 90-120 minute





Left: Exposure therapy involves patients being gradually re-exposed to relevant traumatic events in a progressive and repetitive manner, directed by a clinician.

Above: A PTSD controller interface.

Right: A simulated Humvee IED attack.

sessions over five weeks and is paced by the patient following parameters of general exposure therapy and including outside education and homework around PTSD and exposure therapy. There are a number of research and clinical projects underway within the DoD utilizing Virtual Iraq. Preliminary analysis of the first 20 completers has shown significant reduction in pre-post PTSD symptoms, with 16 of 20 completers experiencing a 50% reduction in symptoms with high levels of patient and provider acceptance and satisfaction.

Bridging Gaps and Improving Services for Rural Veterans in the Four Corners Area: Networking Conference

In order to address issues of mental health care for rural Veterans, TATRC jointly sponsored with the VA Office of Rural Health Defense/Office of Veterans Affairs, a conference in Aurora, CO in April 2009. This conference was hosted by the Four Corners Telehealth Consortium, Veteran's Rural Health Resource Center – Western Region and brought together key stakeholders in the Four Corners region from the VA, DoD, National Guard and Reserves, IHS, and affiliated universities. The purpose of the conference was to increase networking and communication of organizations involved in PTSD/TBI services for Veterans in the Four Corner's region, emphasizing rural Veterans, and addressing rural Veterans' mental health needs and to serve as a catalyst in the further development of telehealth research in the Western United States and beyond.

Four major themes emerged from the conference in this area:

- Sharing information across organizations is vital for raising public awareness and actively demonstrating the benefits of telehealth. By cataloguing research efforts across organizations and building active networks of information exchange, telehealth organizations will have the capacity to reduce redundancy, inefficiencies and gaps in services.
- Identification of best practices will aid in creating uniform guidelines for emerging technologies, such as store-and-forward, videoconferencing and cellular technology.
- Harnessing the power of collaboration is crucial to increasing the political and financial cache of telehealth organizations and their ability to conduct research and evaluations.
- Collaboration presents an opportunity to improve research, share challenges, and explore collective solutions.

A key objective for the conference was to create a forum for exchanging ideas and building relationships between telehealth researchers and other professionals working in this area. A final objective was to leverage these emerging conversations and relationships, having them serve as a catalyst for initiating new research projects and fostering new collaborative partnerships. The conference successfully sparked many sidebar conversations among participants and provides an example to the important support that TATRC provides to the telehealth community in terms of fostering partnerships and telehealth research.

Neurocognitive Baseline Testing for Deploying Personnel

In August of 2008, the DoD implemented neurocognitive baseline testing using the Automated Neuropsychological Assessment Metrics (ANAM4) for all Service Members deploying to theater to serve as the pre-test component of a pre-/post-test comparative medical assessment program to better evaluate mild TBI (mTBI). To date, more than 350,000 ANAM assessments of DoD Service Members have been conducted. The rate of ANAM4 testing is typically 5,000-6,000 personnel worldwide per week and rapidly growing. TATRC has supported the University of Oklahoma Center for the Study of Human Operator Performance (C-SHOP) for advanced ANAM research and development. C-SHOP is the sole source for all ANAM assessment software and system configurations for the DoD Neurocognitive Assessment Test (NCAT) "baseline" program. C-SHOP provides unique expertise to the US Army ANAM Program Office in the areas of hardware and software configuration, data management and analysis, logistical support, subject matter expertise on ANAM development and application, and training.

'Until recently, our whole idea of fitness stopped at the neck. Now, thanks to new breakthroughs in brain science, we are discovering key ways to build a healthy brain and to repair brain injury and disease."

Sandra Bond Chapman, PhD
Director of Center for BrainHealth

Throughout 2009, the ANAM Program Office and the Defense and Veterans Brain Injury Center (DVBIC), assisted by C-SHOP, has provided NCAT/ANAM test training workshops for ANAM familiarization, administration, and interpretation throughout 2009. These workshops have provided training for hundreds of DoD test administrators and healthcare providers worldwide involving all armed services, active duty and reserves. In addition, presentations or demonstrations of the ANAM assessment test were conducted at the International Meeting of the American Telemedicine Association, the Council of College and Military Educators Meeting, the DoD Worldwide Meeting, the National Athletic Trainer's Association Meeting, and the National Academy of Neuropsychology.

The extended potential of ANAM is being realized as many major medical research and rehabilitation hospitals, civilian behavioral health clinics, businesses and industries, and other government agencies are adopting the ANAM test system for many medical, research, and applied applications.

Innovative Assistance Technology to Enhance Rehabilitation for Wounded Warriors

The Assistive Technology Research at the National Rehabilitation Hospital (NRH) is a long-standing congressional that has through-

Right: A hand in the linkage, with emphasis on the 3 contact points and the Velcro straps that attach the fingers to the links of the exoskeleton. Below: The ARMinIII exoskeletal robot. Photo courtesy of the ETH and University of Zürich, Switzerland.

out the years contributed extensively to the body of knowledge in many areas of rehabilitation. Some highlights include:

Kinematics of Reach for the Upper Extremity (UE) Amputee during Functional Task Performance

The results of this study illustrated the importance of training with the provision of a prosthetic arm. Improvement in outcome measurement scores and raw speed highlight the impact training has on prosthesis use. Increasing our understanding of prosthesis use and non-use programs will allow us to implement training and interventions that may decrease rejection rates associated with upper-limb prosthetics.

Robotic Exoskeleton For Post-Stroke Hand Neuro-Rehabilitation

The development of the ARMinIII Robot which is a tabletop, powered exoskeleton for finger flexion/extension that 1) accommodates full range of motion of the fingers, 2) has enough power to assist hands with moderate to high levels of flexor hypertonia, 3) is highly backdrivable, and 4) can apply precise assistance torque to the fingers. This device is an excellent test-bed to evaluate the effectiveness of a variety of control modes for neurorehabilitation (i.e., tone-compensation mode). The ARMin III robot has been installed at NRH and is operational. Further development is underway.

Development of an Over-ground, Pneumatically Actuated Body-weight Support System

Developed and patented the ZeroG is a revolutionary over-ground gait training system that will enhance therapeutic outcomes in individuals following neurological injuries such as stroke, spinal cord injury, and traumatic brain injury, as well as with individuals with amputations of the lower extremities.

COL Barbara Springer, the Director of the Proponency Office for Rehabilitation & Reintegration demonstrating the Zero G.

Developing a Strategic Direction for the Resilience and Reintegration Portfolio

TATRC convened a one-day meeting focusing on research priorities related to resilience and reintegration, specifically mTBI and Warriors in transition. The attendees were military and civilian stakeholders that work in rehabilitation focusing on returning to life roles, psychological health, and community re-integration. The attendees' backgrounds were a balance between researchers and clinicians. The meeting resulted in a consensus of research priorities that will advance the calibre of military rehabilitation services for mTBI and Warriors in transition, and the establishment of a task force to continue developing and implementing an action plan that moves research priorities to military programs.

Military Relevant Rehabilitation Research Priorities for mTBI and Warrior Transition

Research designed to →	IMPROVE		
	REHABILITATION for injuries	REINTEGRATION to family, work, community	RESILIENCE health and wellness
Implement data-driven programs and services	Describe self-reported needs, concerns of soldiers, soldiers' family members, and military context		
	Describe characteristics of service members in WTU		
Establish reliability, validity, normative data on existing instruments:	Vision, visual perception		
	Fatigue		
Develop and validate new performance-based (functional) assessment protocols that evaluates soldier proficiency in:	Productive time use/management		
	Cognitive functioning		
	Initiation of cognitive compensatory strategies		
	Driving		
	Return to duty		
	Dual task performance		
	Managing varying environmental, task demands		
Evaluate the effectiveness of interventions related to:	Remediation of vision deficits	Adaptation for vision deficits	
	Training in dual task performance		
	Return to driving		Return to community mobility
	Activity-based pain management approaches		Self-regulation
	Return to duty training		Maintain duty training
	Life skills training: anger, stress , fatigue, sleep and time management and resuming family roles		
Evaluate the effectiveness of novel treatment media involving use of:	Assistive technologies (smart videogames/simulations)		
	Tele-rehabilitation technologies		
	Animal-assisted therapy		

Trauma

This portfolio focuses on the acute phase of trauma. Care in the field, enroute care, far-forward surgical care, and fixed hospital care are all represented. The projects reflect cutting-edge advancements in the forward care of the injured Warfighter.

Current projects include medical equipment and devices, remote biomonitoring sensors, products for resuscitation such as IV fluids, and agents designed to prevent tissue damage. There are several projects focused on immediate wound care to prevent infection and to control bleeding. It includes training and simulation specific to first responders, physicians, nurses, and allied health providers. Additionally, intra- and inter-theater telemedicine as well as surgical robotics are also included.

In subsequent years, TATRC will continue to fill gaps identified by the individuals responsible for the initial treatment of those injured in theater. Specific areas include advancing first responder care, improving techniques for open wound care, enhancing surgical technologies, and increasing the effectiveness of deployable technologies, from portable sensors and monitors to reach-back systems for physicians operating in austere environments.

Development and Validation of the Intravenous Membrane Oxygenerator

The goal of the proposed research program is to produce a platform of clinical quality respiratory support devices for the treatment of respiratory failure in Warfighters and civilians. The University of Pittsburgh Artificial Lung Laboratory has invented, refined, and tested three respiratory support devices: the Respiratory Support Catheter (RSC); the Percutaneous Respiratory Assist Catheter (PRAC); and the Paracorporeal Respiratory Assist Lung (PRAL). ALung Technologies has licensed the technology associated with the RSC, PRAC, and PRAL, and ALung Technologies and the University of Pittsburgh Artificial Lung Laboratory will jointly perform the studies.

The benefits to the DoD at the completion of this program are the creation of multiple respiratory support

A patient on PRAL.

Portfolio Team

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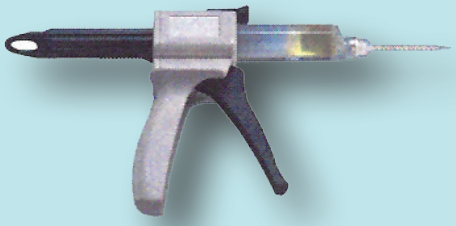
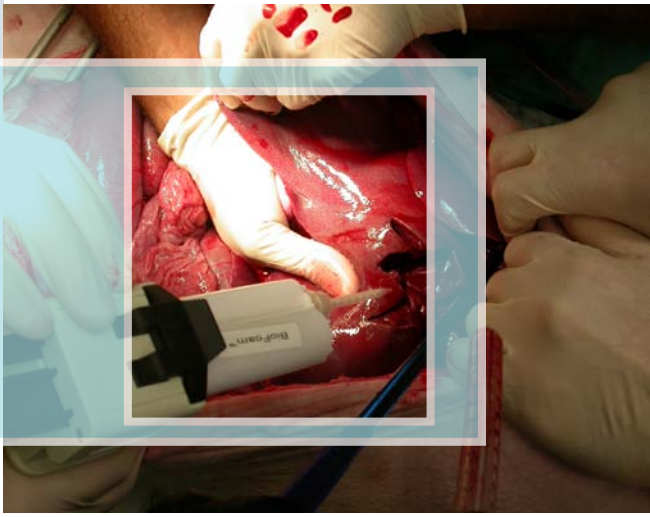
Dr. Thomas Knuth
Nita Grimsley
Philip Zakas
Dr. Ken Curley (RAD II)

The Portable Handheld Pneumothorax Detector is being used in animal studies at USAISR.





devices for the treatment of Warfighters with respiratory failure, and the existence of a US company capable of producing these devices.

One goal of the research and development program is to produce a platform of clinical quality respiratory support devices for the treatment of respiratory failure in Warfighters and civilians. The creation of the PRAL will allow for oxygenation and CO_2 removal in severely injured patients until adequate lung function returns. This strategy will potentially decrease the "died of wounds" rate of severely injured patients.

Left: Demonstration of the intended use of the product. Below: Solid models developed to demonstrate size, shape and weight characteristics.

Non-Invasive Pneumothorax Detector

Pneumothorax is an accumulation of air in the pleural cavity, often as the result of a blunt trauma causing a partial collapse of the lung. While a pneumothorax is easily treatable, it can become life threatening if not detected at an early stage. Current methods for diagnosing pneumothorax (chest x-ray, chest CT scan) are not possible for battlefield medics and not practical for long-term monitoring of critical care patients. It is especially important for first responders to properly diagnose and treat a pneumothorax when an airlift evacuation is considered, as the reduced pressures could result in an expansion of the pneumothorax and death. A portable handheld pneumothorax detector that is inexpensive, accurate, and non-invasive would be a great benefit.

Working with Lawrence Livermore National Labs, ElectroSonics Medical, Inc. (EMI) has developed prototype pneumothorax detection devices based on patented Micropower Impulse Radar (MIR) technology. This device emits very low power radio frequency impulses of a very high frequency and broad spectrum (1-4 GHz). The resultant echoes are collected by extremely high-speed circuitry and analyzed by a proprietary software algorithm. EMI has demonstrated the ability of these devices to accurately detect the presence or absence of a suspected pneumothorax in over 40 patients at two metro-Detroit hospital emergency departments. The unit's current form-factor is about the size of two decks of cards stacked on top of each other, and can be operated using any device that has a USB port and can run the software.

Protein Hydrogel for Use in Trauma

This project proposes to provide Forward Surgical Team (FST) and Combat Support Hospital (CSH) with an expandable hemostatic agent as a packing material for Damage Control Surgery. Upon application, the liquid hemostat becomes an adhesive foam, creates a mechanical barrier against blood, and secures the side by adhering to the surrounding tissue. The objective of this effort is to provide the Warfighter, medic, and combat surgeon with a hemostatic agent that is effective, easily applied, lightweight, easily transported, generates no heat, and has so special storage requirements. A protein hydrogel formulation that meets such a criteria (BioFoam) has been identified and patents have been applied for the formulations and the uses. It needs to be further developed for battlefield use, including FDA approval. This material will initially be developed for use during Damage Control Surgery at the FST or CSH level. It is anticipated that its use will later be broadened to include medic- or self-administration, and use on the extremities.

New Sprayable Liquid Wound Dressing

Researchers are developing a new, sprayable liquid wound dressing technology that an injured Warrior could apply one-handed in a combat setting. The spray forms a tough hydrogel in seconds that conforms directly to the wound without sticking to it when removed.

The GelSpray™ Liquid Bandage forms a tough hydrogel in seconds that conforms directly to the wound without sticking to it when removed.

The GelSpray™ Liquid Bandage was approved by the US FDA for minor cuts and irritations in 2008. With TATRC's assistance, its developers are preparing for a human clinical study required to extend the technology to battlefield care. The technology shows promise for quicker wound healing with less care required.

"GelSpray offers significant clinical advantages: The thick, protective film limits bleeding, absorbs wound fluids and directly transports medication to the entire wound bed. It does not significantly adhere to the wound bed—unlike most other dressings, where there is re-bleeding or delayed healing due to removal of granulation tissue whenever the wound dressing is removed."

Dr. Joachim Kohn
Rutgers University, Department of Chemistry
Wright Laboratories

Neurotrauma

Molecular Determinants Fundamental to Successful Axonal Regeneration after Spinal Cord Injury

Investigators at St. Thomas University are using a zebrafish spinal cord injury model in vitro *and* in vivo *to better understand the mechanisms that gourn the success and failure of axon regeneration after spinal cord injury.*

Basic research to discover how to promote nerve axon regeneration may lead to new possibilities for restoring function in those paralyzed due to spinal cord injuries. In 2009, Dr. Jeffery Plunkett began a project at St. Thomas University to use a zebrafish spinal cord injury model system to discover genes and molecular mechanisms crucial for successful axon regeneration.

Plunkett explains, "Growth-inhibitor proteins are produced at the injury site, and thus axons do not regenerate in mammals. Some zebrafish brainstem neurons do grow axons across a spinal cord injury, even in the presence of such proteins. Identifying the genes crucial to this differential ability will lay the foundation for translational research to mammals."

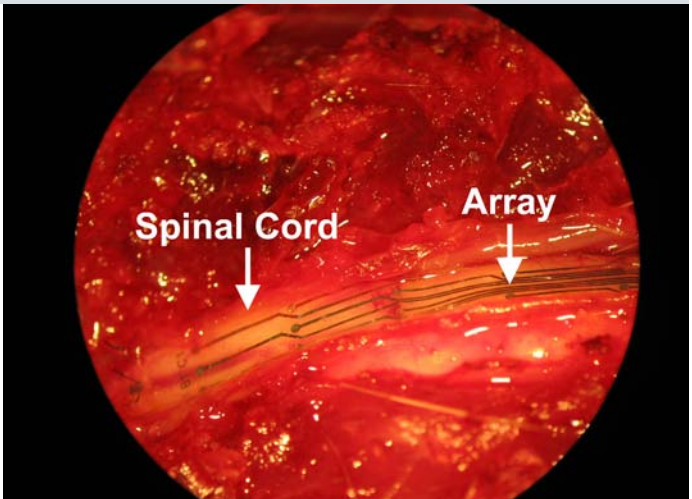
To move basic science closer toward application, and to encourage minority participation in the neurosciences, Plunkett has established a minority student research consortium between St. Thomas and the University of Pittsburgh School of Medicine. He has also gathered a group of international experts in the field to consult on the experiments.

Electrode Array Development for Recovery of Stepping Following Spinal Cord Injury

Dr. Reggie Edgerton and Dr. Joel Burdick of the University of California, Los Angeles (UCLA) are leading the way in applying the concept of central pattern generators to recover the ability to walk after spinal cord injury. Central pattern generators are neural networks in different parts of the nervous system that can produce rhythmic patterns of behavior such as walking or breathing without rhythmic sensory or central input.

Edgerton says, "The spinal cord can do more than we think. If we can find just the right place and way, we can stimulate the central pattern generator in the spine for locomotion and use the

Investigators at UCLA have developed a high density electrode array implant that can enable stepping in spiral cord injured rats. They are now tailoring the system for use in human clinical trials.



Portfolio Team

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Dr. Brenda Bart-Knauer
Dr. Eugene Golanov
Dr. Eva Lai
Cody Straub
Jennifer Blumberg

"We are seeking to understand what stimulation does biologically in terms of promoting nerve regeneration and recovery, and why some patients improve so much more dramatically than others... Many who show the most improvement are in the military or very athletic."

Dr. John McDonald
Kennedy Krieger Institute

undamaged spinal circuitry to continue to produce stepping behavior, even though the circuitry is separated from brain control. We aren't inducing, but enabling stepping with epidural stimulation; we are changing the responsiveness of the spinal cord to the sensory input from the legs so that input can initiate and control stepping.

The team's work, thus far in rats and cats, is showing that robotic physical training along with an implanted long-term electrode array for epidural stimulation is most effective in restoring the ability to step and bear weight.

TATRC is supporting the team's effort to refine the high-density electrode array system in animal models in order to move to human clinical trials in 2010.

Advanced Restoration Therapies in Spinal Cord Injury

The most effective rehabilitative therapy to date for injury-related paralysis is activity-based therapy with functional electrical stimulation (FES) of the muscle, a technique pioneered in this country by Dr. John McDonald's team at the International Center for Spinal Cord Injury, Kennedy Krieger Institute. In most patients, bone density improves and bedsores decrease; some patients even walk again.

FES became an official standard of care in physical therapy for the lower extremities in 2006. With TATRC's support, McDonald is bringing its benefits to injured service members. The funding supports pilot training workshops on the theory and practice of activity-based restorative therapy (ABRT) for rehabilitation professionals in the military and VA.

In addition, the team is conducting the necessary validation and safety studies to promote FES as an accepted therapy standard in regaining function in the arms as well.

The team began human clinical trials of FES-assisted ABRT for the upper extremities in the fall of 2009.

A technique pioneered by investigators at the Kennedy Krieger Institute is restoring function to those with spinal cord injuries.

Advanced Prosthetics

Advanced Prosthetics

www.tatrc.org/prosthetics

As a result of a meeting at WRAMC in Washington, DC in 2003, TATRC established the Advanced Prosthetics and Human Performance Research (APHP) Portfolio. During that initial meeting at Walter Reed, three main priorities were expressed—a military all-in-one foot, a comfortable socket, and a dexterous hand. In direct support of those priorities, and working hand in hand with care providers and patients at WRAMC, Brooke Army Medical Center (BAMC), and Naval Medical Center in San Diego (NMCSD) the focus of this portfolio is on advanced prosthetics, orthotics, assistive devices, treatments and interventions for patients with major limb amputations, fractures, and other orthopædic related injuries. This portfolio also includes outcome and program assessment studies and administers the MARP, including intra-DoD research which is often referred to as the Military Amputee Intramural Research Program (MAIRP).

Research funded and managed through the APHP Portfolio directly supports the Clinical and Rehabilitative Medicine Research Program (CRMRP) (https://crmrp.amedd.army.mil).

Military Foot

Army Medicine strives to enable an injured Warfighter to return to duty status as soon as possible. Within their desires and capabilities, a Warfighter who has experienced limb loss is no exception. Traditional prosthetic legs tend to accommodate low-speed activities, such as walking. However, in order to return to the field on active duty, or to return to an active civilian life, service members need a prosthetic leg that is able to perform during rigorous activities and under extreme conditions such as swimming, climbing, or running on uneven, wet, or sandy terrain.

The ideal "military foot" is not a simple problem as every patient's circumstances are unique and require what is essentially a custom solution. Lower limb amputations are generally categorized as trans-femoral (above the knee, or AK) or trans-tibial, (below the knee, or BK). Other levels of amputa-

Nearly half of all amputees experience some kind of phantom limb pain. This is thought to be the result of the brain misinterpreting signals, or lack thereof, from the affected region. During a study funded out of the Military Amputee Intramural Research program, Dr. Jack Tsao enrolled participants in a trial to use the mirror therapy technique 15 minutes a day, five days a week, for four weeks. Pain levels generally began to come down after the first week and continued diminishing with treatment. Every single person who used the mirror experienced relief, and some reported that their phantom pain disappeared altogether.

Portfolio Team

Troy Turner
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tion include ankle, knee, and hip disarticulations. There are a variety of solutions which incorporate passive or active knee and ankle joints which can be controlled by an onboard computer or system of myoelectric devices.

As a primary area of focus within TATRC's Advanced Prosthetics and Human Performance Research Portfolio, TATRC is fostering a broad range of lower-extremity (LE) related projects to support our service members as they strive to achieve their highest possible quality of life. A number of examples follow:

Powered prosthetic devices have made it easier for amputees to perform everyday tasks than ever before. The next step for these devices is ruggedization so that we can return a greater percentage of our wounded service members to duty. TATRC is working with Otto Bock to develop vastly improved capabilities, and deploy a ruggedized version of Otto Bock's microprocessor controlled prosthetic knee known as the C-Leg.

- With TATRC funding, Otto Bock is developing a version of the C-Leg which is hardened, and ruggedized, with enhanced durability, increased strength, significantly longer battery life, field recharging features, secure electronic function, which is field serviceable and patient adjustable.

- KCF Technologies of State College, PA is developing an energy scavenging device as a component in the ankle of a lower extremity prosthetic limb. The component will be designed and demonstrated on a C-Leg in collaboration with Otto Bock USA. This energy scavenging component will capture and store energy during normal activities such as walking and running. The captured energy will automatically recharge the batteries of the C-Leg. This energy will greatly extend the operational time of a battery charge, and possibly eliminate the need for battery charge altogether.

- Dr. Tom Sugar's team at the Arizona State University Human Machine Integration Lab is building a new generation of smart, active, energy-storing, and dynamically tunable, transtibial prostheses. The current goal is to support linear walking at user-selected speeds. A control scheme will be developed to identify when the user wants to start and stop the prosthesis, and it will automatically speed up or slow down the prosthesis as walking speed is increased or decreased.

- Dr. Hugh Herr at The Massachusetts Institute of Technology Media Lab is building a powered lower extremity prosthesis for transfemoral and transtibial amputees. A soleus-like actuator will be used to power ankle movements, and a gastrocnemius, bi-articular mechanism to augment knee flexion during terminal stance. In the soleus-like actuator, a spring will be placed in series with a motor, and the spring stiffness will be set equal to that of the Achilles tendon. A gastrocnemius, bi-articular mechanism will be included in the transfemoral prosthetic leg design, and will comprise a tendon-like spring in series with an electromagnetic clutch. After early stance knee flexion, when the knee undergoes an extension phase, the clutch will engage and elasticstrain energy will be stored in the series spring. That stored energy will then augment rapid knee flexion during terminal stance, lifting the ankle-foot prosthetic mass from the ground surface with an electromagnetic clutch. The second part of the study is to perform biomechanical and energy consumption studies on amputee patients with these devices.

- The Rehabilitation Institute of Chicago is attempting to tie all of these technologies together by developing a neural-control interface for prosthetic legs. This will involve designing a neural interface which will control

both cyclic activities, as well as independent movements of the prosthesis. A large degree of control will likely be available from the normal residual limbs of transfemoral and transtibial amputees. Outlying phases will include the development and implementation of targeted muscle reinnervation (TMR) surgery for people with lower limb amputations. This will provide increased neural control information for a prosthetic leg. The ultimate goal is the application of these technologies to a powered ankle, powered-knee, and an integrated powered ankle-knee prosthetic system.

Comfortable Socket

Amputees may use a variety of ways wrap their residual limb within the socket to make themselves more comfortable, or less uncomfortable as the case may be. For a suction socket the most common method is to wrap the residual limb in one or several socks. The limb is then compressed with a gel liner which provides cushioning between the limb and the hard-shell socket, and enhances suction between the prosthesis and the residual limb. Once the limb is inside the liner and socket, a polymeric gel sleeve is then placed over the socket, extending up onto the limb to secure the vacuum which holds the socket onto the limb. This configuration, even during low intensity activities, can cause sweating. The sweating will lead to slipping between residual limb and the socket/sleeve. The increased movement in the socket could lead to rashes and blistering a well as loss of vacuum integrity.

There are a variety of ways to make the socket more comfortable. Improved gel liners and more padding within the socket are simple solutions. TATRC is funding several research efforts examining both active and passive methods of decreasing discomfort/increasing comfort, eliminating intra-socket moisture, and maintaining intra-socket vacuum.

- Sandia National Laboratories is developing a socket monitor that senses and records pressures and minute changes in pressure between the limb and the socket. This is being accomplished using MEMS (micro-electromechanical systems) to measure pressure on small air/silicon-filled bladders arranged throughout the socket which may also be able to be used to enhance socket fit. This liner would be able to be used for both upper extremity (UE) and LE prostheses, and could be a permanent part of the socket.
- The Ohio Willow Wood Company is assessing methods for using standard socket shapes and customizable liners for shortening the amount of time to fabricate a prosthesis for a transtibial amputee and to extend the useful life of a prosthesis.
- The University of Wisconsin, College of Health Sciences has designed a project to ensure that pressure remains the same irrespective of the environment and the activities performed in a definitive prosthesis stump-socket interface. They also seek to estimate an all-round patient-specific performance index for the socket design.

Above: John Fergason, Chief Prosthetist at the Center for the Intrepid at Brooke Army Medical Center, images a Soldier's residual limb to ensure optimal socket fit.

Left and Right: Creating the perfect socket is as much art as science, though current TATRC-funded research is changing that and ensuring a wounded Warrior's comfort and improved limb health.

- Infoscitex Corporation of Waltham, MA has two SBIR projects which relate to socket comfort. Both projects feature a multilayered socket that takes advantage of a novel braided material for strength and passive conformability with thin layers dedicated to wearer comfort. This new socket provides ultimate fit for improvement in the performance of the prosthesis. The socket adapts itself to the changing physical shape of the residual limb as the prosthesis is worn. The materials are lightweight, breathable, and ultrasound transparent, allowing the prosthesis to function in a variety of environments.
- Physical Optics Corporation in Torrance, CA is developing a new Liner and Electroactive Polymer Prosthetic Socket (LEAPPS), based on lightweight polymers that respond to externally applied electrostatic forces. LEAPPS incorporates an array of rectangular electroactive polymer cells that function as individually controlled force actuators to dynamically adjust the socket fit. Capacitive sensors positioned within each cell relay the physical displacement of the actuator to an embedded microcontroller, enabling rapid compensation for external stresses and changes in musculature. An innovative multiple-layer socket liner, utilizing active peristaltic motion and hydrophilic wicking fibers, provides a comfortable fit and efficient moisture management.

Dexterous Hand

UE prosthetic devices require strength and dexterity, but do not regularly carry as heavy a load as do LE devices. A prosthetic arm should be strong enough to carry a heavy load, fast enough to catch a ball, and precise enough to pick up a pen or loose change. Our service members need a dexterous hand to pull the trigger of a weapon, or play the piano. A hand that can perform all of these tasks is not currently available, and for this reason it is impossible for many upper limb amputees to return to duty or to a desired quality of life.

In 2005, DARPA dedicated a large amount of funding toward the Revolutionizing Prosthetics Program. According to the DARPA website (www.darpa.mil), "the Revolutionizing Prosthetics Program will create, within this decade, a fully functional (motor and sensory) upper limb that responds to direct neural control. This revolution will occur by capitalizing on decades of previous DARPA investments in neuroscience, robotics, sensors, power systems, and actuation. In particular, this program builds on the Defense Sciences Office (DSO) Human Assisted Neural Devices Program, which has recently decoded the brain's motor signals with such fidelity that motor movements of a robotic arm can be achieved entirely by direct brain control."

DARPA's significant investment in UE devices has allowed TATRC to focus on the priorities of LE devices and socket comfort and functionality.

The Outcomes and Program Assessment Program

As advances are being made in prosthetic device technology, an increasing number of researchers are focused on assessing the quality of life of returning Veterans with traumatic injuries/amputations. The Outcomes and Program Assessment program within the Advanced Prosthetics and Human Performance portfolio is comprised of multiple qualitative and quantitative studies, interviews, focus groups, surveys, and program evaluations aimed at bettering the quality of life for many Veterans. Instead of researchers assuming they know the needs of the amputee population, they are determined to understand these issues from the Veterans themselves.

Indiana-Ohio Center for Traumatic Amputation Rehabilitation Research

"I know the loss of my leg changed, probably, the course of my life; but I guess I made the best of it and redefined my goals."

Quote from an oral history in the Inidana - Ohio study

Photo courtesy of: Derek McGinnis/The Modesto Bee

The objective of this research effort is to assess the long-term physical and psychosocial outcomes of traumatic amputations due to conflict. Vietnam War Veterans with traumatic amputations have over 30 years of experience living with an amputation; however, no database was in existence to garner information from this population. The Indiana-Ohio Center for Traumatic Amputation Rehabilitation Research identified this as a problem and has established a database of around 450 Vietnam Veterans who sustained war-related amputations. The team is currently conducting interviews with a subset of this database to ascertain certain themes in the oral histories. These themes will help to focus the quantitative instruments to be distributed to all of the enrolled participants. The information collected from the research will be made available to Vietnam Veterans, caregivers, people involved in treating and caring for military personnel with traumatic amputations, and policy makers to optimize care of this cohort and prepare to care for others experiencing a combat related amputation.

Military Amputee Intramural Research Program (MAIRP)

TATRC's APHP Research Portfolio administers the MAIRP, which is a subset of MARP and closely linked with the US Military Amputee Patient Care Program (MAPCP). The MAPCP is a congressionally funded clinical service and part of the Department of Orthopedic Surgery & Rehabilitation at the Walter Reed Army Medical Center. The primary aim of the MAIRP is to establish and support research initiatives that will advance amputee clinical patient care strategies and prosthetic technology used to optimize patient recovery after traumatic limb loss. The MAIRP is unique in that it provides a vehicle for intramurally funded efforts which has allowed clinicians at locations such as WRAMC, BAMC, and NMCSD to conduct research that will ultimately improve the quality of life of service members with limb loss.

The MAIRP received congressional funding in the amount of $10.25M from fiscal year 2005 through 2007. An executive committee of clinical and research experts was established to determine research priorities and play an integral role in determining which projects receive funding. The Henry M. Jackson Foundation was identified as the Research Management Organization responsible for establishing the infrastructure for MAIRP initiatives, assisting with research protocol development, facilitating acquisition and management of resources and funds, and ensuring regulatory compliance.

The MAIRP is a major keystone within TATRC's Advanced Prosthetics and Human Performance portfolio. Clinicians who work with amputee patients on a daily basis are able to see gaps in current practice standards and are invited to propose research to bridge these gaps through MAIRP funding. This includes examining mobility issues, gait training analyses, and comparing outcomes of specific prosthetic devices.

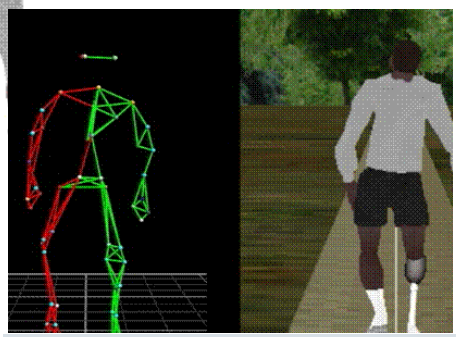
Development of the Comprehensive High-level Activity Mobility Predictor (CHAMP)

OIF/OEF service members who have sustained traumatic amputations frequently demonstrate physical capabilities beyond those measured by currently available assessment tools. Therefore, this MAIRP project intends to develop a reliable measure of functional mobility in military amputees who are able ambulate independently; predict the ability of military amputees to perform high-level functional mobility activities; differentiate among levels of ability; measure the changes in ability;

and determine the relationship between high-level functional mobility and level of limb loss. Overall, the tool could be used to assess the amputee service member's readiness to return to higher level activities and return to duty. The 7-item CHAMP instrument was developed and implemented in May 2008 and 97 active-duty servicemen between the ages of 19-39 based at Fort Bragg participated in reliability and validity testing of the instrument. These normative test scores for able-bodied service members will serve as a comparison for service members with lower extremity amputations to be completed in Phase II of the CHAMP study.

Amputee Gait Training Using Virtual Reality and Real-Time Feedback

While working in the gait lab at Brooke Army Medical Center, Dr. Jason Wilken noticed significant gait deviations in service members who have experienced transtibial or transfemoral amputation in spite of extensive gait training. Access to the Computer Aided Rehabilitation Environment (CAREN) system has allowed the development of a virtual reality based gait training environment using real-time feedback. The VR environment and real-time tracking and display within the scene have also been successfully completed. Normative data have been collected and follow-up patient data are now being collected. Preliminary findings include a 15% reduction in metabolic cost and improvements in frontal plane trunk motion symmetry. Patient training data are being completed and publication of the results is planned.



Above: Real-time display of patient gait data.

Right: Personalized avatar for visual feedback during the virtual reality gait training.

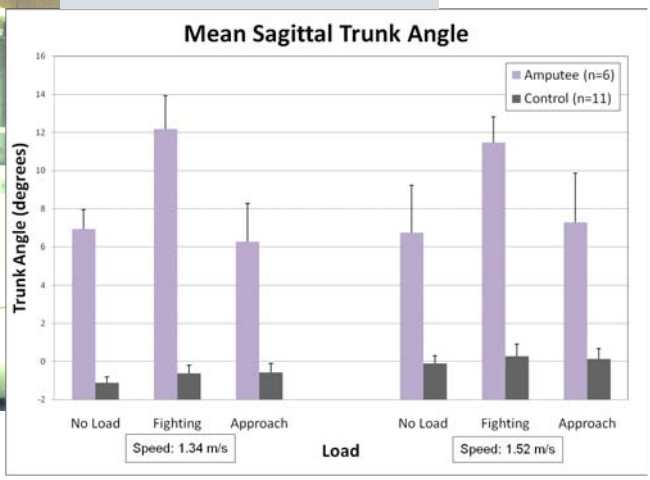
Baseline data using able-bodied service members is collected for the CHAMP Phase II effort.

Biomechanical and Metabolic Analysis of Amputees Carrying Military Loads to Meet Return to Duty Requirements

The amount of energy one exerts during activity is influenced by many factors, including amputation, co-morbidities, and training. For military service members with traumatic amputations who want to return to active duty, the energy expended while performing fundamental Warfighter tasks is likely even greater. Due to advances in military technology, average loads carried by dismounted Warfighters have tripled upwards of 41 kg since the 18th century and therefore require a high metabolic cost.

Ms. Barri Schnall, MPT at the Center for Performance, and Clinical Research Manager at WRAMC envisioned a study in which the findings would help the physical rehabilitation community to better understand the nature and extent of the physical demands placed on lower extremity amputee service members. The study will quantify the ability of service members with unilateral, transtibial amputations (TTAs) to carry loads and meet US Army Warfighter Performance Standards. Preliminary findings indicate that those with TTAs have more asymmetric step lengths than the control group. It has also been noted that the stance percentage is notably higher on the sound limb of those with TTAs. Also, the control group walked upright in all conditions while those with TTAs increased for-

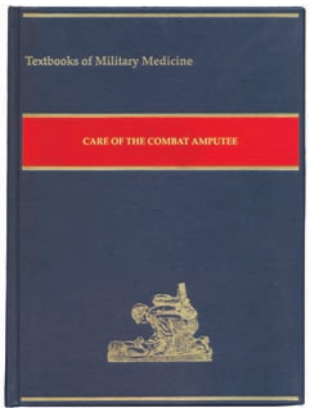
Data collection has included 12 uninjured control subjects and 11 subjects with trans-tibial amputations.



ward lean, most markedly when wearing a "fighting load."

Rehabilitation of the Combat Amputee Consensus Conference

A three-day symposium—Rehabilitation of the Combat Amputee Consensus Conference— held at the Center for the Intrepid, BBAMC, in Fort Sam Houston, TX in September 2007 has resulted in the soon-to-be-released publication titled Care of the Combat Amputee. This unique event was organized by the Human Engineering Research Laboratories (HERL), Director Dr. Rory Cooper and COL Paul Pasquina, MD, Medical Director of the Amputee Care Program at WRAMC, and was supported by a grant from TATRC.



Book jacket for "Care of the Combat Amputee."

The event united military, VA, and civilian amputee care and rehabilitation experts with a goal to establish consensus on standard-of-care issues, as well as to facilitate identification of interest areas for further clinical, technical, translational and developmental research. Lecturers from wide-ranging specialties and institutional backgrounds contributed to group educational sessions. Symposium attendees participated in both large and small specialty group discussions: Programs and Systems Practices; Surgical Management and Planning; Special Medical Considerations; Physical Rehabilitation and Therapeutic Interventions; and Prosthetic Devices and Assistive Technologies.

Before the symposium, attendees drafted chapter content, which was discussed and brought to concurrence during specialty breakout sessions. HERL graduate students and Borden Institute editorial staff facilitated chapter development both on-site and subsequently, resulting in the production of a 28-chapter, 731-page book. This work was completed during a time of war, with the ongoing arrival of wounded Warfighters to military and Veteran medical centers, as well as the establishment of new programs, expansion of benefits, and rapidly changing medical care. Ultimately, this publication will serve as a reference for experienced clinicians; a textbook for students, residents, and fellows; a source for researchers, and an historical document.

Programs such as the WRAMC Firearms Training System (FATS) allow Service Members, like Adam Kisielewski of TATRC, to rehab and retrain using Warfighter-specific tasks.

Regenerative Medicine

This portfolio addresses the challenges of rebuilding Warfighters following injuries, often severe, and generally sustained during combat. Currently, there are more than 70 active projects, totaling more than $115M in investments. Funding and management of these projects has paved the way for many investigators to understand the military challenges in developing innovative medical treatments for traumatic injuries. In 2007, TATRC supported the USAMRMC, including the RADs and USAISR, on its first major initiative in advancing innovative medical treatments for wounded Warriors with its successful launch of the Armed Forces Institute of Regenerative Medicine (AFIRM) in 2008.

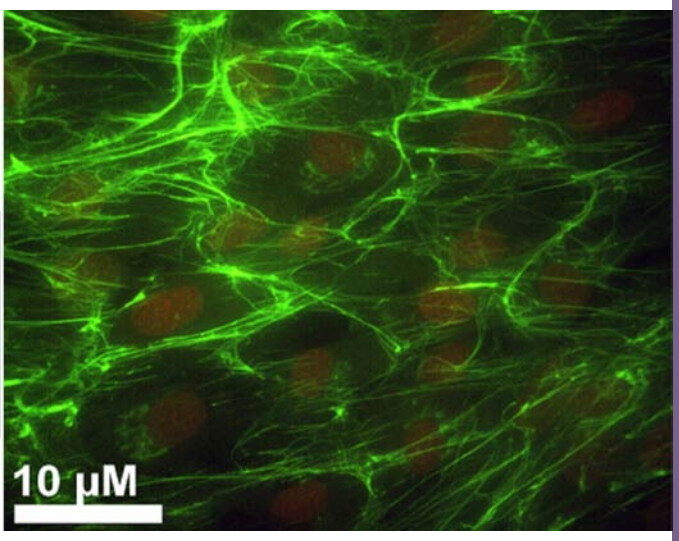
TATRC continues to identify areas of unmet military medical challenges by analyzing the overall Army medical research investments in regenerative medicine. In addition, TATRC works with its funded research partners to develop solutions that TATRC has identified as technical gaps and/or advantages to augment its research portfolio, and the Army medical portfolio. Regenerative medicine and tissue engineering concepts offer an attractive option to develop novel treatments to restore tissue and function compared to forced amputation in addressing critical medical challenges.

There remains a large number of critical research areas for which regenerative medicine and tissue engineering could have a huge impact on the medical outcome for injured Warfighters. These include regeneration of large complex, organized tissue that will integrate with the body and provide function, development of novel strategies for rapid cell generation to create functional, engineered tissue and/or for cell therapies, and translation of information from basic studies in cell biology and inflammation to make regenerative medicine and tissue engineering viable solutions.

Several potential approaches are highlighted here.

Controlling the Body's Responses toward Functional Healing and Regenerative Medicine

An area of identified critical knowledge gap is to understand how inflammation affects tissue healing and translating this knowledge to engineering a solution where cells can be reprogrammed from inflammation signals to start the healing process versus cell death and/or scarring. Researchers at the Benaroya Research Institute based in Seattle, Washington are taking on this challenge to find ways to control inflammation, with the goal to develop new therapies to regulate these natural reparative processes, specifically to



Immunostaining for Type I collagen in 10-day cultures of LDXN. (Image courtesy of Thomas Wight, Benaroya Research Institute, with permission from the American Society for Investigative Pathology.)

Regenerative Medicine

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redirect the body's responses to injury toward functional healing and regeneration. In particular, the investigators are looking at how to utilize signaling mechanisms to regulate inflammatory and fibrotic processes to direct cell behavior and orchestrate tissue repair in acute and chronic disease. For example, studying the role of the matricellular protein HEVIN, and its role in inflammation and wound repair, could help understand the factors that regulate inflammatory processes and use this information to guide the development of novel therapeutic treatments aimed at manipulating cellular trafficking to direct healing responses toward defined positive outcomes. As a case in point, a unique population of T cells was found that respond to acute inflammation and then elaborate chemokines to attract further inflammation-suppressing cells to migrate to the site, a natural mechanism for the resolution of inflammation that might be exploited therapeutic use (see Koch MA et al. The transcription factor T-bet controls regulatory T cell homeostasis and function during type 1 inflammation. *Nature Immunology* 2009; 10(6): 595-602).

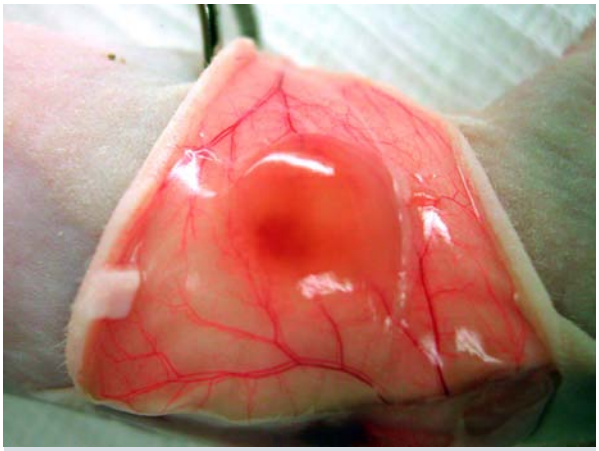
Enhancing Wound Healing in a Variety of Tissue Injuries

Burn trauma remains one of the highest combat injuries resulting from IED exposure and one where medical intervention is labor intensive and expensive and medical outcome inadequate. Stemnion, Inc. (Pittsburgh, PA) is funded through USAMRMC TATRC to develop novel stem cell based therapies using amnion-derived multipotent progenitor cells to address burn injury, and in addition spinal cord injury, and traumatic brain injury. These amnion-derived multipotent progenitor cells are formed very early in embryonic development from the same embryonic cell layer that forms the fetus. Thus, these cells have strikingly similar characteristics to embryonic stem cells, but possess important characteristics that distinguish them from embryonic stem cells and adult stem cells. One of these characteristics includes defined cell growth, meaning they do not grow and multiply indefinitely; thus they are not considered immortal. This characteristic substantially reduces the risk of transplanted amnion-derived cells forming spontaneous tumors following transplantation. Also, these cells are readily available and easily harvested without any ethical issues associated with embryonic stem cells. Further, amnion-derived multipotent progenitor cells exhibit a unique combination of properties known to be associated with wound healing including extensive cell proliferation potential, differentiation into multiple cell types, and secretion of cytokines and many growth factors. Stemnion is taking on the challenge to develop and bring to the market an innovative wound healing agent based on the byproducts of amnion-derived multipotent cells for treatment of burns. The TATRC funded research allowed the company to generate data for filing an IND and now the first phase of clinical studies are being conducted through investors' funding. Through TATRC coordination, the company is also working with other TATRC funded partners as well as the Walter Reed Army Institute of Research (WRAIR) to evaluate the neuroprotective and neurorestorative effect of amnion-derived multipotent progenitor cells for spinal cord injury and for TBI. It is anticipated that the transplanted cells will produce growth factors and cytokines in the damaged area; thereby enhancing the survival of injured neurons, and potentially replace lost neurons. If successful, such therapies could substantially change the lives of patients suffering from spinal cord injury or TBI.

Generating Microvasculature that will Support New Tissues Formation

TATRC is funding research to address a technological barrier in tissue engineering and regenerative medicine, specifically how to provide oxygen and nutrients to implanted engineered tissue. Dr. Joyce Bischoff and co-investigators at the Children's Hospital Boston have developed a robust *in vivo* model for blood vessel formation using human endothelial progenitor cells (EPCs), isolated from peripheral or cord blood, and mesenchymal stem/progenitor cells (MPCs), isolated from adult bone marrow or cord blood. The *in vivo* model uses immune-deficient mice in order to avoid immune attack on the human cells. The most recent peer-reviewed research, published in Circulation Research (Melero-Martin et al., *Circ. Res.* 2008; 103: 194-202), demonstrates that a perfused vascular network can be established *in vivo,* via implantation of these two cell populations. As noted in the accompanying editorial, this

research provides "a significant step forward in the vascularization process necessary for tissue engineering and regenerative medicine." The paper was awarded a 2009 Best Manuscript Award from the journal Circulation Research. Creation of a microvasculature network that is connected with the host is necessary to support new tissue formation and tissue implantation/engraftment because the supply of oxygen and nutrients is vital to the cells that make up the tissue. Demonstrating an extensive and functional microvascular network connected with the host blood supply is a significant achievement. Furthermore, that this is achieved through the use of adult autologous human progenitor cells, obtained through a minimally invasive procedure, is another important milestone.



Macroscopic view of expanded Matrigel plugs seeded with EPCs and MPCs showing formation of vascular networks in vivo. *(Image courtesy of Dr. Joyce Bischoff, Children's Hospital, Boston MA.)*

Developing Solutions to Address Craniofacial Injury

Another identified area of unmet medical challenges is healing craniofacial injury. TATRC is taking a multi-pronged approach that includes funding projects focusing on developing innovative, moldable scaffolds to recreate facial structure and developing an analyzable database with injury coding tools as a prelude to planning/optimizing reconstructive intervention. For example, David Puleo, Ph.D. and colleagues at the University of Kentucky are investigating multifunctional materials to treat traumatically induced orthopedic and craniofacial injuries. Since war injuries are often found contaminated with debris and subsequently microbes, from which even an indolent infection initiates a chronic inflammatory response that undermines tissue repair, there is a need to develop materials that both eliminate bacteria and regenerate injured tissues. The team is designing a moldable, biodegradable bone graft substitute that will provide localized, controlled, sequential release of antimicrobial and osteogenic agents for repair of large orthopedic and craniofacial injuries. It is anticipated that delivery of an antimicrobial agent directly from the osteogenic defect filler will result in improved and accelerated bone healing as compared to either individual treatments alone or bone grafting in conjunction with systemic antibiotics. For the craniofacial injury coding database, TATRC is funding SimQuest LLC (Silver Spring, MD) to tackle this area in collaboration with investigators at WRAMC and TATRC assigned subject matter experts from USAISR. Since craniofacial reconstruction is a complex process that requires multiple surgeries and results are often not aesthetically pleasing or functional, it is anticipated development of a searchable database containing past craniofacial surgeries on combat casualties and tools to encode the case information could be used to understand the effects of differing injury mechanisms and treatments on facial wounds and restorative care.

Moldable bone filler. (Image courtesy of David Puleo, University of Kentucky.)

Nano-Medicine

Nano-Medicine

The Nano-medicine and Biomaterials Portfolio is focused on identifying novel developments in nanotechnology, materials science, Micro-Electro-Mechanical Systems (MEMS) systems, and biomaterials that can address significant problems in military healthcare. These technologies have the potential to provide new drugs and devices for diagnosis and treatment of a wide range of clinical problems. Nanotechnology investigates the properties of materials at very small scales. At these small sizes common elements such as gold, silver, carbon, silicon, and titanium acquire unique properties that are radically different than those properties found in the bulk material. Within this portfolio, investigators are applying nanotechnology to improve drug delivery, develop novel bio-compatible materials, and build new biological scaffolds.

The Nano-medicine Portfolio supports other TATRC portfolios including: Biosensors, Regenerative Medicine, Infectious Disease, and Imaging. This interplay of research fields can be seen in Dr. Song Li's work found in the Regenerative Medicines Portfolio. Dr. Li (UC Berkeley) has been developing nano-fibrous scaffolds for drug and stem cell delivery applied to spinal cord regeneration. The team employs this scaffold to help bridge gaps in a spinal cord lesion, guiding axon growth and regeneration.

Nanotechnologies allow for precise investigations of cellular processes, enzyme reactions, and tissue response to injury. Both Nano and Micro technologies can be applied to the fabrication of biomaterials that mimic tissue. These constructs can be used to replace lost bone and other tissues. These biomimetic materials encourage the growth of cells, the integration of bone into implants, and the regeneration of nerves after traumatic injury. Three projects are highlighted from this portfolio.

Alliance for NanoHealth (ANH)

One project representative of this portfolio is the center developed by Dr. Mario Ferrari at the University of Houston called the Alliance for NanoHealth (ANH). This highly interdisciplinary consortium of seven institutions was established to advance nano technology for a broad range of applications, including cancer therapy and drug delivery. The ANH is using its current funding for:

- imaging and hyperthermia treatment of inflamed endothelium;
- nanotechnology applications in vascular grafts; and
- targeted delivery of nanoparticles for anti-tumor therapies.

In addition, the ANH is supporting 10 seed projects to evaluate the application of nanotechnology for clinical proteomics, molecular imaging of neurological diseases, targeted RNA therapies for drug resistant cancers including lung cancer, studying biological dynamics of solid cancers, prosthetic sensors for improved rehabilitation, central nervous system therapeutics and axon regenerative scaffolds, 3D sensors for neural recording, and multiplexing MRI diagnostics. Each of these center and seed projects were selected from 25 proposals submitted to the ANH. The proposals were evaluated on their scientific merit, potential impact, technical approach, and investigator qualifications. This

Portfolio Team

Dr. Warren Grundfest
Elias Wilson

project demonstrates the broad range of research in the Biomaterials and Nano-medicine Portfolio.

Combat Wound Initiative

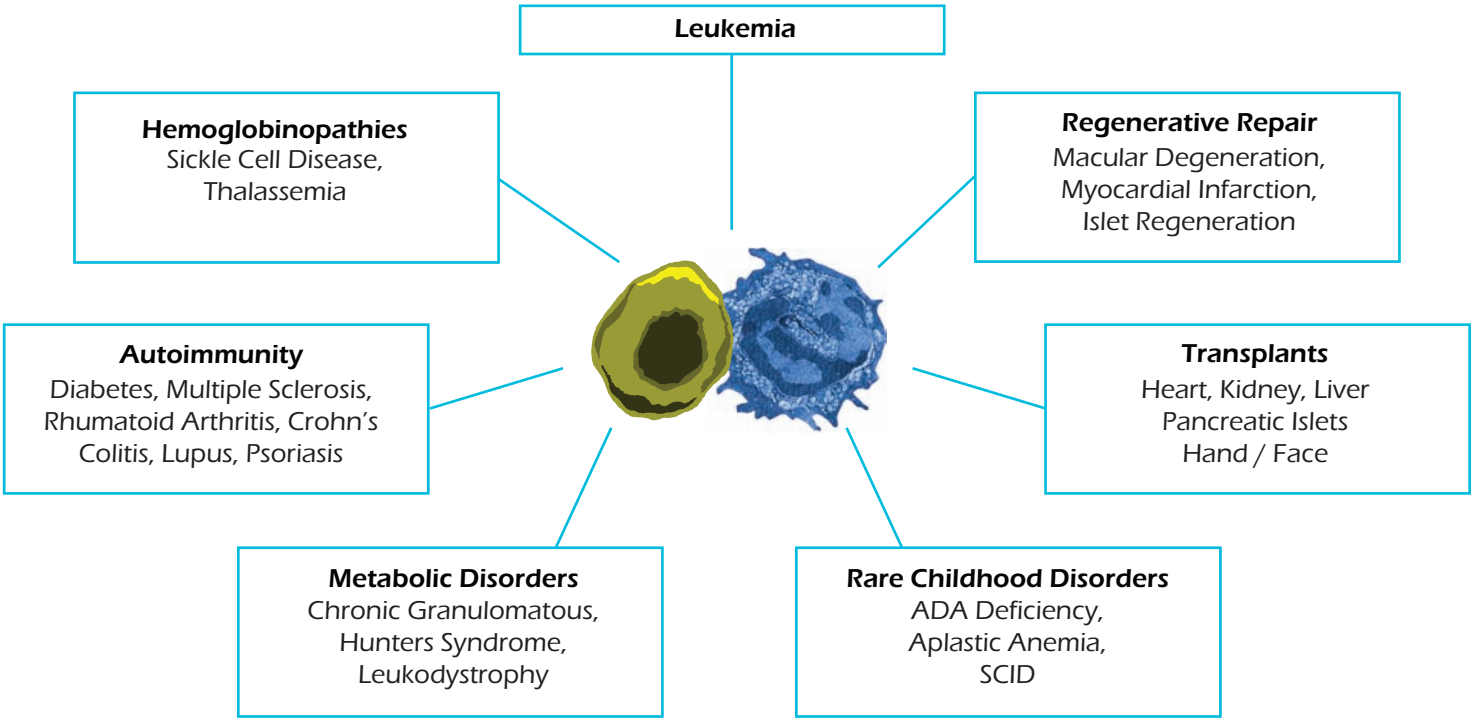
This project is developing a bio-repository of tissues and fluids collected from a wide range of infected and non-infected wounds. These samples are examined for bio-makers to investigate the molecular mechanisms which effect wound healing. Preliminary data suggest that these cytokines bio-markers can predict which wounds will heal and which wounds will need additional therapeutic intervention. This research has been presented at Advanced Technology Applications for Combat Casualty Care (ATACCC) conference.

Facilitating Cell Transplantation Research

The portfolio also contains a unique transplantation research project which investigates the role of the facilitating cell in promoting immune tolerance. This research suggests that modulation of the immune response is possible and can be used to overcome problems of rejection and graft verse host disease that are common in complex tissue transplantations. Studies in patients with sickle cell disease have established that facilitating cell therapy can induce chimerism in these patients. The sickle cell trait is treated using donor bone marrow, which is tolerated by the recipient patient, dramatically treating the sickle cell disease.

The figure below illustrates the conditions and disorders which could benefit or be cured by bone marrow/facilitating cell transplants derived through this research.

Conditions that could Benefit from or be Cured by a Bone Marrow/Facilitating Cell Transplant



This Bone Marrow/Facilitating Cell Transplant study has the potential to help with the treatment or curing of many diseases and disorders. This study also presents a novel process to allow for new sources of tissue donors, which can help repair or replace vital functions within the body (i.e., Islet of Langerhans). This figure identifies the areas where this study has the potential to advance the method of treatment.

Key Programs & Partners in 2009

This section on "key programs and partners" represents TATRC investments that explore new models of medical research innovation and for building research capabilities based on unique offerings of a particular region (e.g., ANH, CIMIT, HFHCN), institution (e.g., CASIT, NCIRE), or on a network of organizations linked through a common problem set (e.g., cancer genomics, NETPR, Samueli Insititute, vision research).

In each of the examples we have chosen to highlight this year, there is a very significant DoD benefit, as well as a larger public purpose to developing these capabilities. These programs highlight TATRC's central theme of partnering across different types of organizations and disciplines in cooperative center-like teams that can provide agile and sustainable responses to DoD medical problems. These evolved organisms are very different than a collection of individual science project grants, with purpose-focused activity.

Other notable successes in this class of cooperative center-like grants, not specifically highlighted in this section, are the Pennington Biomedical Research Center and the Imaging Science and Information Systems (ISIS) at Georgetown University that was synergistic in the development of TATRC.

Alliance for NanoHealth (ANH)

www.nanohealthalliance.org

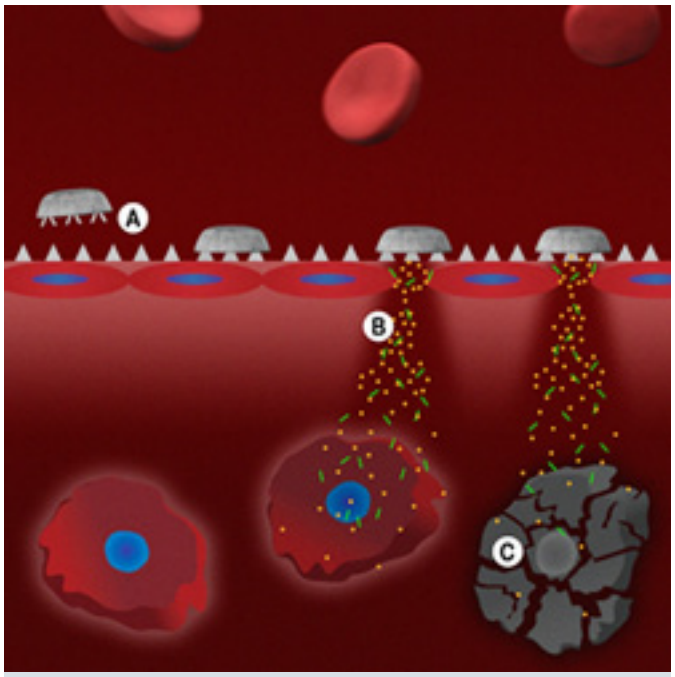
Leading the Applications of Nanotechnologies to Medicine

The Alliance for NanoHealth (ANH) is the first multi-disciplinary, multi-institutional collaborative research endeavor aimed solely at using nanotechnology to bridge the gaps between medicine, biology, materials science, computer technology and public policy. The mission of the Alliance is to collectively bridge the disciplines to develop nanotechnology-based solutions to unresolved problems in medicine. Its principal goal is to provide new clinical approaches to saving lives through better diagnosis, treatment, and prevention.

The ANH comprises eight world-class research institutions located within the world's largest collection of healthcare facilities, namely the Texas Medical Center and the greater Houston region. Member institutions include:

- Baylor College of Medicine
- University of Texas M.D.
- Anderson Cancer Center
- Rice University
- University of Houston
- University of Texas Health Science Center at Houston
- Texas A&M Health Science Center
- University of Texas Medical Branch
- The Methodist Hospital Research Institute

ANH institutions are committed to developing and applying nanotechnology-based tools in the battle against heart disease, cancer, diabetes, stroke, and infection. The willingness to leverage expertise and infrastructure within the consortium of institutions facilitates the formation of new scientific associations that provides a rich collaborative foundation



One major concept ANH has been developing is the use of Nano-Porous Silicon-Based Multi-functional Microparticles (A) to target specific endothelia markers, directing the release (B) of therapeutic nano-particles, to treat/kill unwanted cells (C) within a specific region.

upon which the ANH has established a wealth of research and development opportunities.

Since the Alliance's inception in 2004, the ANH has received funding from the State of Texas and the US Congress. Over $20 million of funding has been utilized for:

- Infrastructure development & shared equipment;
- Seed grant funding for high-risk collaborative research projects;
- Planning grants intended to prepare multi-institutional teams for future Center of Excellence funding opportunities;
- Seminars, workshops, & conferences;

ANH FAST FACTS FY05 - FY08

200 Journal and Conference Publications
6 National meetings and workshops
10 Seminars
25 Supported Projects
7 Key Technologies

Congressional Year	Funds	Contribution	Researchers	Graduates/Post Doctorates
2009	$2,724K	Inter-institutational grant competition for research projects in nano medicine (supports an estimate of 9 seed grants and 2 pre-center grants).	29	16
2008	$3,394K	Inter-institutational grant competition for research projects in nano medicine (supports 10 seed grants and 3 pre-center grants).	31	18
2007	$934K	ANH Planning Grant Program (preparing interdisciplinary, multi-institutional, teams for future centers of excellence opportunities); and purchase of critical equipment.	18	2
2006	$1,768K	Interdisciplinary research; and equipment purchase.	7	9
2005	$2,352K	Funding of 10 seed grants following an inter-institutional competition (60 pre-proposals, 34 full proposals).	36	18

TATRC funding from FY2005 to FY2008 has already actively engaged over 85 researchers from the 8 ANH Member Institutions, 15 researchers from outside the ANH, and enabled collaborative interactions with at least 6 industry partners.

- Undergraduate student summer internships with ANH institutions;
- Graduate student scholarships;
- Fellowships for post-doctoral researchers; and
- Recruitment of world-class nano-bio researchers.

FDA-ANH Nanotechnology Initiative (FANTI)

The FDA partnered with the ANH comprising eight academic institutions in the Greater Houston, Texas Region. This new collaboration is called the FDA-ANH Nanotechnology Initiative - FANTI. The goal of FANTI is to develop a framework to help transition nanoengineered medical technologies (pharmaceuticals, biotechnologies, medical devices) from pre-clinical stages of development to FDA commercial approved technologies. In developing this framework, FANTI seeks to identify high-priority scientific and translational gaps in moving nanoengineered medical products from pre-clinical stages of development to and through clinical phases.

ANH Sponsored Workshops & Conferences

One of the first activities under FANTI, was a two-and-a-half-day scientific workshop that was held in March 2008 in Houston, TX. The first two days of the Workshop were devoted to the identification of translational gaps and challenges in nanoengineered medical product development, along with an accompanying set of projects aimed at bridging such gaps. As FDA jointly sponsored this Workshop, these discussions were informed by regulatory input from senior FDA staff—all with the ultimate goal of stimulating innovation in nanotechnology and informing medical product development. The final half-day was reserved for the presentations of the project concepts, and other findings as appropriate, to key stakeholders (i.e., finance, industry leaders, patient advocate foundations, etc.) to seek input on a final list of project recommendations. A summary of this workshop was captured in the publication: "Seven Challenges for Nano-medicine" in the *Journal of Nature Nanotechnology* (May 2008).

The ASME Nanotechnology Council and the ANH is organizing the First Global Congress on Nano-Engineering for Medicine and Biology (NEMB2010) held in 2010 in Houston, TX.

Shared Equipment for the Advancement of Biomedical Nanotechnology Research provided through the TATRC Grants

High-pressure freezer for cell and tissue specimen and transfer systems.
A Fluorescence Molecular Tomography instrument (FMT) System to conduct non-invasive tomographic visualization and quantification of near infrared fluorophore labeled nanoparticles and quantum dots.
A Pathway Bioimager System.
A Fluorimetric imager & associated workstation, software and interfaces, and high throughput temperature and computer controlled 2D gel generator for high-throughput fluorescent two-dimensional difference gel electrophoresis (2D DIGE) proteomic analysis.

From FY 2005 to FY 2008, the ANH has been allocated over $3.8 million in funding for shared equipment. In many instances, this funding represents a part of the overall purchase, running and maintenance costs. This shared equipment for the advancement of biomedical technology research was provided through TATRC grants.

NEMB2010 focuses on the integration of Engineering Sciences, Mechanical Engineering and Nanotechnology to aid in addressing fundamental problems in Biology and Medicine and in developing devices for the early detection, imaging and cure of diseases.

The FDA and ANH held the 2nd FDA-ANH Nanotechnology Initiative Scientific Workshop in May at the George R. Brown Convention Center located in Houston, TX. The intent of this event was to build upon the outcomes of last year's workshop in Houston and to develop the strategic plan for implementation of this Public-Private Partnership (PPP) that was outlined in the recently published Memorandum of Understanding (MOU) among FDA and the eight academic members of the ANH, (http://www.fda.gov/oc/mous/academic/225-07-8006.html). Furthermore, the purpose of this meeting was to obtain feedback from key stakeholders on the recommended initial projects for implementation and potential resources to be leveraged under the PPP. Representatives from government, industry, and academia presented key elements and considerations to address 1) biodistribution of nanoparticles, 2) nanomaterial periodic table, and 3) characterization/standardization of nanoparticles, which were identified as top opportunities and ripe for collaboration at last year's meeting.

Alliance for Nanohealth Representative Publications

Tasciotti E, Liu X, Bhavane R, Plant K, Leonard AD, Price BK, Cheng MM, Decuzzi P, Tour JM, Robertson F, Ferrari M. "Mesoporous silicon particles as a multistage delivery system for imaging and therapeutic applications." *Nature Nanotechnology*. 2008; 3: 151-157.

Serda RE, Gu J, Bhavane RC, Liu X-W, Chiappini C, Decuzzi P, Ferrari M. "The association of silicon microparticles with endothelial cells in drug delivery to the vasculature." *Biomaterials*. 2009; 30: 2440-2448.

Serda RE, Gu J, Burks JK, Ferrari M. "Quantitative mechanics of endothelial phagocytosis of silicon microparticles." *Cytometry*: Part A 2009; 5: 752-60.

Serda RE, Ferrati S, Godin B, Tasciotti E, Liu X, Ferrari M. "Mitotic trafficking of silicon microparticles." *Nanoscale*. 2009; 1: 250 - 259.

Decuzzi P, Godin B, Tanaka T, Lee S-Y, Chiappini C, Liu X, Ferrari M. "Size and shape effects in the biodistribution of intravascularly injected particles: A preliminary study." *J Control Release*. [Epub ahead of print], Oct, 2009.

Cancer Center of Excellence & National Functional Genomics Center

www.tatrc.org/Proteomics-Genomics

Establishing Personalized Medicine Genomics Networks for the DoD

The Genomics/Proteomics Portfolio was formed in 2007 and envelops fundamental areas of genomics and proteomics research. The success of this portfolio lies in the development of collaborative efforts to share existing resources, such as bioinformatics data systems and tissue repositories, in order to create exciting scientific accomplishments that can be applied in the ongoing development of personalized medical treatments for our Warfighters and their families.

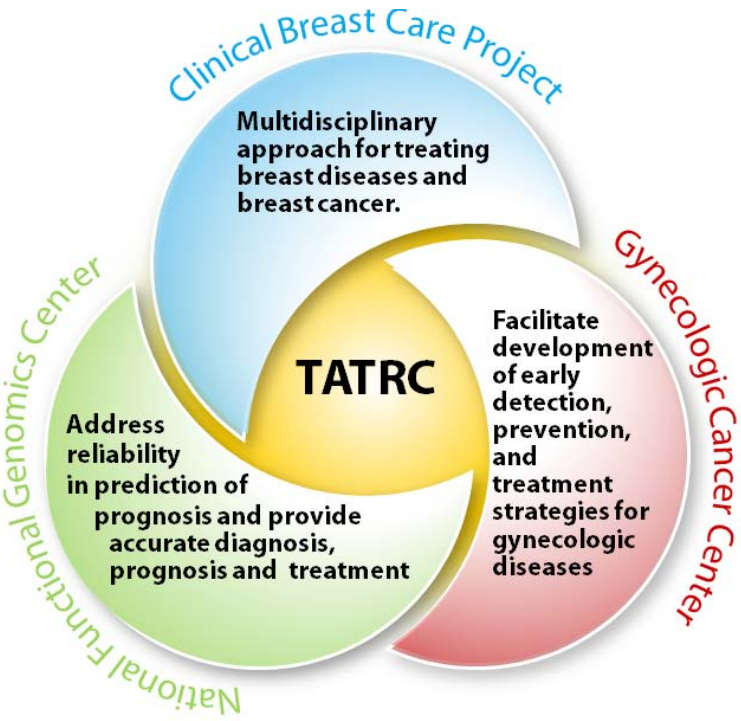
The Clinical Breast Care Project (CBCP), the Gynecologic Cancer Center (GCC), and the National Functional Genomics Center (NFGC) represent three major programs within the Genomics/Proteomic Portfolio that have demonstrated excellence in science, resource sharing, and collaboration of subject matter experts to bring advances in scientific research from the laboratory bench to the patient's bedside.

These TATRC programs have shown the value and the crucial need for scientific partnership efforts within the research community in order to reduce and eliminate the predominance of cancer and other diseases in our society. Collaborations allow forward thinking and reduce duplicative efforts that can waste money, time and valuable resources. These programs have shown outstanding leadership in establishing collaborative partnerships.

CANCER CENTER OF EXCELLENCE FAST FACTS FY01 - FY09

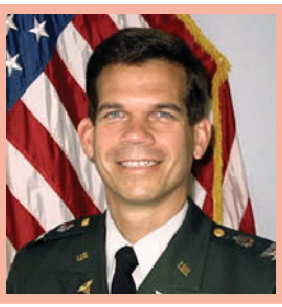
- 4 Patents
- 76+ Publications
- 19 Collaborators
- $18,707,101 in Funding for FY09

The Value of Collaboration



Clinical Breast Care Project at Walter Reed Army Medical Center (CBCP)

The Windber Medical Center (WMC)/WRAMC CBCP has helped to lead the way into the 21st Century in the crusade against breast disorders. The project has utilized a multidisciplinary approach as the standard of care for treating breast diseases and breast cancer. This multidisciplinary model integrates prevention, screening, diagnosis, treatment and continuing care; however, the project is further unique in the incorporation of advances in risk reduction, informatics, tissue banking and research. These efforts will focus on decreasing the morbidity and mortality of breast cancer among American women.



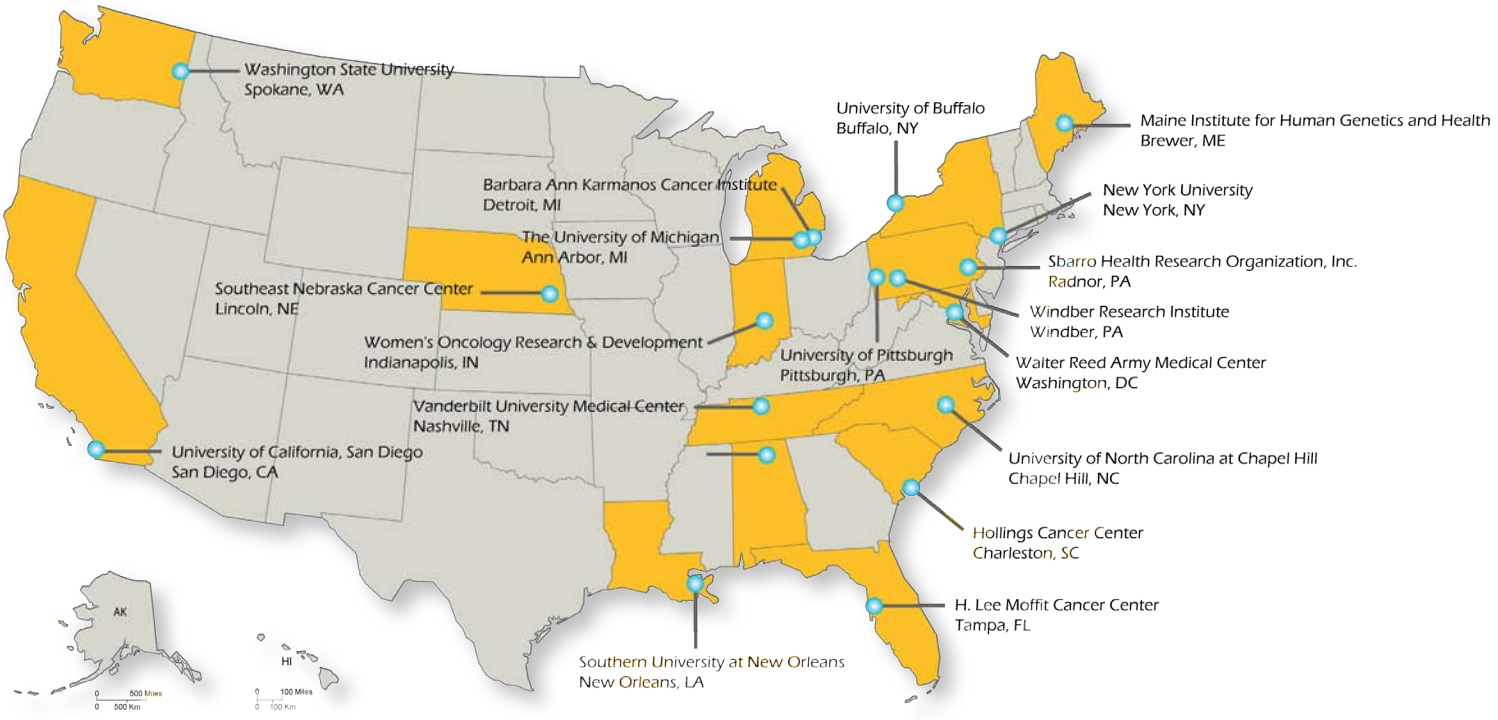
"The CBCP is crusading against breast disorders through prevention, diagnosis, treatment and research."

COL Craig Shriver, M.D.
Principal Investigator
Director, Clinical Breast Care Project

The CBCP, led by COL Craig Shriver, MD, has been a TATRC recipient since 2005. Dr. Shriver and his team's goals include:

- Decreasing the morbidity and mortality of breast cancer among American women.
- Developing a comprehensive breast care center/system to enable health care providers with a multidisciplinary team approach that works towards the common goal.
- Empowering women with breast cancer and other breast disorders with the decision-making tools and environment to enhance quality of life and to meet psychosocial needs of the patients and their families.

The CBCP is the outcome of Congressional appropriations and consists of extensive collaborative effort between Windber Medical Center and WRAMC. The scientific accomplishments that have been ascertained from this program has allowed the CBCP to transition to core funding and in FY10 the CBCP will be a part of the President's Budget, an accomplishment that will allow the continuation of this program.



The 2009 Genomics/Proteomics portfolio comprises of a wide array of genomics and proteomics research that extends from coast to coast.

Gynecologic Cancer Center (GCC) at WRAMC

The focus of gynecologic cancer investigators at WRAMC is to characterize the molecular alterations associated with benign and malignant gynecologic disease and facilitate the development of novel early detection, prevention measures, and treatment strategies for the management of gynecologic disease. The objective of this program is to reduce the incidence, morbidity, and mortality of gynecologic diseases among our active duty Service Members, female dependents, and other military health care beneficiaries. Improved gynecologic health, particularly among the female active duty population, is critically important for the maintenance of readiness among a military force that is composed of an expanding female component.

The GCC, led by COL Larry Maxwell, MD, has been a TATRC recipient since 2004. Funds received during GCC's beginnings were devoted to the design and construction of the Gynecologic Disease Center at WRAMC, which was completed in 2005. This center of excellence serves both clinical and research functions in providing cutting edge gynecologic cancer care to military healthcare beneficiaries.

Once the infrastructure was in place, the GCC began to establish and maintain collaborations with other gynecologic researchers. Today, the collaborations through the GCC keep growing. The scientific accomplishments that have been achieved from this program have allowed the GCC to begin receiving Program Objectives Memorandum funds (POM)—meaning in FY10 the GCC will be a part of the President's Budget.

The Value of Shared Resources

CBCP uses facilities, resources and expertise at the Uniformed Services University of Health Sciences (USUHS), the WRAMC, the WMC and the Henry M. Jackson Foundation.

As the CBCP transitions from Congressional Special Interest funds to program objective memorandum (POM) funds, the collaborations that have been formed will remain and continue to expand into exciting and distinctive areas of breast cancer research.

GCC: 2009 and Beyond

In the United States, approximately 80,000 women annually are diagnosed with gynecologic cancer and almost 27,000 women are expected to die from the disease. The negative impact of gynecologic disease on the female component of our nation's military forces is continuing to grow. The development and expansion of a partnership focused on gynecologic disease continues to provide novel information that is being translated into prevention and treatment strategies to improve the quality of life for women with gynecologic disease while reducing the economic impact on military and civilian health care systems.

"The Gynecological Disease Program seeks to advance the prevention, diagnosis, and treatment of gynecological diseases to improve health outcomes for women."

COL Larry Maxwell, M.D.
Principal Investigator
Director, Gynecologic Cancer Center

Major CBCP Scientific Accomplishments 2004-2009

Clinical Care

• Clinical Care built state-of-the-art breast care facilities at the Windber and Walter Reed sites. The Walter Reed Breast Center opened on July 31, 2001, and the Joyce Murtha Breast Center at Windber on February 21, 2002.

Tissue Banking

• Established tissue banking at both for acquisitions, storage, and movement of tissue from all breast surgeries being performed at both locations for research purposes.

Risk Reduction

• Developed breast disease database collaboration between Walter Reed and Windber, in close collaboration with leading industry leaders in the high-end database field.

Informatics

• Established a screening program to identify women who are at high risk of developing breast cancer, and to enter them into a very time- and resource-intensive risk reduction program to decrease significantly these patients' chance of getting breast cancer in the future.

Focused Research

• Investigated breast cancer vaccine development with breast cancer vaccine offered at both sites.

• Conducted functional genomic/microarray/proteomics global expression profiling analysis of acquired tissues.

• Demonstrated a model of collaborative research in functional genomics established through a high-end microarray, genomics, and proteomics facility at the CBCP Windber Research Institute (WRI).

Major GCC Accomplishments 2004-2009

Early Detection

• Developed the most accurate blood test currently available that can detect both early and advanced stage endometrial cancer (99% accuracy).

• Demonstrated with a sophisticated cost analysis that the molecular profiling test would be cost effective in the screening of the general population in order to detect cancer early; resulting in improved patient outcomes and reduced financial burden to the military health care system.

• Validated this serum-based test case in case control sets; scheduled to undergo Phase III testing using a retrospective longitudinal case control set from a from a prospective cohort.

Molecular Profiling

• Identified gene and protein abnormalities associated with uterine fibroids, which will facilitate development of novel therapeutics towards a disease that is currently managed with surgery.

Risk and Prevention

• Discovered Vitamin D can be combined with hormonal regimens in providing optimal chemoprevention.

• Partnered with Evanston Northwestern and investigators at Harvard associated with the Nurse's Health Study to further investigate these preliminary data.

Treatment

• Obtained FDA approval for several vaccines developed by the GCC and their collaborators aimed at decreasing the likelihood of endometrial cancer recurrence.

The National Functional Genomics Center (NFGC)

The status of oncology care in the United States today can perhaps best be described as "experimental." Even though there is a wide range of accuracy in the diagnosis of many cancers, reliability in the prediction of prognosis for patients is seriously lacking; resulting in variability of treatments rendered, and subjecting patients to tremendous stress during the course of their disease, which in and of itself can complicate treatment. The NFGC was established to address these issues and to provide cancer patients with accurate diagnosis, prognosis, and treatment.

The NFGC, led by Dr. Jack Pledger, has been a TATRC recipient since 2002. Dr. Pledger and his team's research focuses on three interconnected areas: Microarray, proteomics, and drug discovery. These areas of research are tied together-with bioinformatics and support by additional technologies-and are used:

- To discover molecular signatures for cancer;
- To identify cancer markers for early detection and unique therapeutic targets;
- To discover putative new drug therapy targets and develop innovative treatments; and
- Ensure each of these areas of research provide solutions to enable "personalized" medicine.

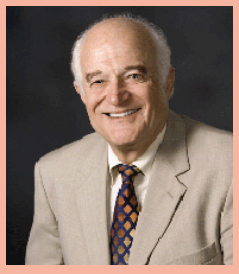
Funds received during NFGC's infancy were used to plan and design new and expanded infrastructure at the Moffitt Cancer Center subsequently to pave the way for state-of-the-art genomics research. Investment in high-quality shared resources staffed with trained technical personnel has shown to minimize the costs of equipment outlay for individual

researchers and maximizes efficiency and reproducibility of research. Early funding efforts also helped to create NFGC's External Advisory Board, chaired by General John Parker, M.D., (former Commanding General at USAMRMC at Ft. Detrick, MD. This board consists of top, internationally recognized, experts in various disciplines of genomics and is designed to oversee the activities of the NFGC and to provide recommendations for its future growth.

Once the infrastructure was in place, the NFGC began to establish and maintain collaborations with other centers; which have directly produced beneficial research to the military and to homeland security. Today, the collaborations through the NFGC keep expanding and the NFGC continues their pursuit to study and validate molecular targets of cancer that predict cancer risk, diagnosis, prognosis, and response to treatment.

"The NFGC is designed to bridge the gap between pure science and patient care by stimulating translational cancer research that will make a real difference in how we diagnose the disease and how we treat it."

W. Jack Pledger, Ph.D.
Principal Investigator, NFGC



Major NFGC Scientific Accomplishments

- Successfully developed a consortium of expert partners who are working to conduct functional genomics research at each institution and collectively through group grant projects, the first joint project started August 2009.
- Licensed an invention directed to the development of a genetic signature into a gene chip used to predict disease stage and to select among therapy options in cancer patients.
- Supported the first-ever clinical trial to use the molecular data from an individual woman's ovarian cancer to select her chemotherapy ("personalized medicine").

The Value of Shared Resources

The NFGC's "Shared Resources" houses specialized equipment and employs trained scientific staff in specific scientific disciplines. The Moffitt Cancer Center contains numerous shared resources that can be used by all investigators; thus, minimizing the costs of equipment outlay for individual researchers and maximizing efficiency and reproducibility. Moffitt's Shared Resources are available to the NFGC's affiliate partners for a fee. The NFGC has been able to provide funds to expand, enhance, or establish Shared Resources at the Moffitt Cancer Center by purchasing equipment and software and making strategic hires of personnel.

Shared Resources that have been supported by the NFGC include but are not limited to the following resources: Analytic Microscopy, Biomedical Informatics, Biostatistics, High Throughput Screening, Microarray, Proteomics, and Tissue Core.

NFGC: 2009 and Beyond

The NFGC remains diligent in their pursuit of quality research. The NFGC continues to serve as a centerpiece of functional genomics research that will validate the theory that cancer has a molecular signature that can be used to accurately diagnose, predict survival, and define an optimal course of treatment for each individual patient. The quality of life for cancer patients will be immensely improved by this novel, personalized approach.

Cancer Center of Excellence Representative Publications

Holliday C, Rummel S, Hooke JA, Shriver CD, Ellsworth DL, Ellsworth RE. Genomic instability in the breast microenvironment? A critical evaluation of the evidence. *Expert Rev Mol Diagn.* 2009; 9(7): 667-78.

Farley JH, Tian C, Rose GS, Brown CL, Birrer M, Risinger JI, Thigpen JT, Fleming GF, Gallion HH, Maxwell GL. Chemotherapy intensity and toxicity among black and white women with advanced and recurrent endometrial cancer: a Gynecologic Oncology Group Study. *Cancer.* 2009; Nov 18. [Epub ahead of print].

Guo JP, Shu SK, Esposito NN, Coppola D, Koomen JM, Cheng JQ. IKK-epsilon phosphorylation of ERalpha-Ser167 and contribution to tamoxifen resistance in breast cancer. *J Biol Chem.* 2009; Nov 23. [Epub ahead of print] . PubMed PMID: 19940156.

Mani RS, Tomlins SA, Callahan K, Ghosh A, Nyati MK, Varambally S, Palanisamy N, Chinnaiyan AM. Induced Chromosomal Proximity and Gene Fusions in Prostate Cancer. *Sciencexpress.* 29 October 2009. DOI: 10.1126/science.1178124.

Erin H. Seeley and Richard M. Caprioli. Molecular imaging of proteins in tissues by Mass Spectroscopy. www.pnas.org_cgi_doi_10.1073_pnas.0801374105.

Patents:

Turkson, James; Sebti, Said M.; Guida, Wayne; Yip, Man Lun; Lawrence, Nicholas; Lawrence, Harshani; Greedy, Benjamin. Small molecule inhibitors of STAT3 with antitumor activity. PCT Int. Application WO 2007 136858 Moffitt's Office of Technology Management and Licensing is in the early stages of license discussions with 3 separate groups.

Javier Torres-Roca and Steven Eschrich: A non-provisional patent and corresponding PCT were filed by the Moffitt Cancer Center on Sept 12, 2008. Serial No. 1½10,135, "Gene Signature for the Prediction of Radiation Therapy Response" and Serial No. PCT/US200%76311, "Gene Signature for the Prediction of Radiation Therapy Response". The patented technology has recently been licensed under an Option Agreement (Sept 9, 2009) to Cvergenx.

The Center for Advanced Surgical and Interventional Technology (CASIT)

www.casit.org

Pioneering Bioengineering Solutions for the Future of Healthcare

The David Geffen School of Medicine at UCLA was founded during Dr. E. Carmack Holmes' tenure as Chairman of the Department of Surgery as a program to utilize the resources of the School of Medicine, School of Engineering, and other assists of UCLA to advance the technology of interventional medicine.

The mission of CASIT is to define and advance the state-of-the-art of surgical and interventional technology and to modernize surgical education and training. To achieve this mission CASIT's goals are to deliver novel surgical and interventional therapies to patients, to develop greater interventional capacity through robotics, informatics, and simulation, to improved accuracy and precision in the performance of minimally invasive procedures, and to identify new technologies which will facility development of new interventional procedures.

CASIT is a specific UCLA-designate research center housed in a state-of-the-art 3,700 sq. ft. research facility. The center includes the Gonda Robotic Center, a wet research laboratory, a telecommunications center, a computer simulations facility, an integrated operating room suite, and administrative offices. The concept of CASIT also includes the existing highly developed research programs in microelectronics, micromachining and nanofabrication in the Department of Biomedical, Mechanical, and Engineering at UCLA. The CASIT operation room served as a test bed for the design of the Operating Room (OR) at the new UCLA Ronald Regan Hospital. This new 550-bed UCLA hospital provides the opportunity to bring all of these resources together in the OR of the Future. Based on the CASIT investigations, the hospital assigned 100,000 sq. ft. to the new ORs and interventional suites which work as an integrated facility. The use of CASIT as a design and model test bed enhanced and facilitated development of the new operating rooms. CASIT also helped to design the ICUs, recovery rooms, and other vital parts of the new hospital.

CASIT FAST FACTS FY04 - FY08

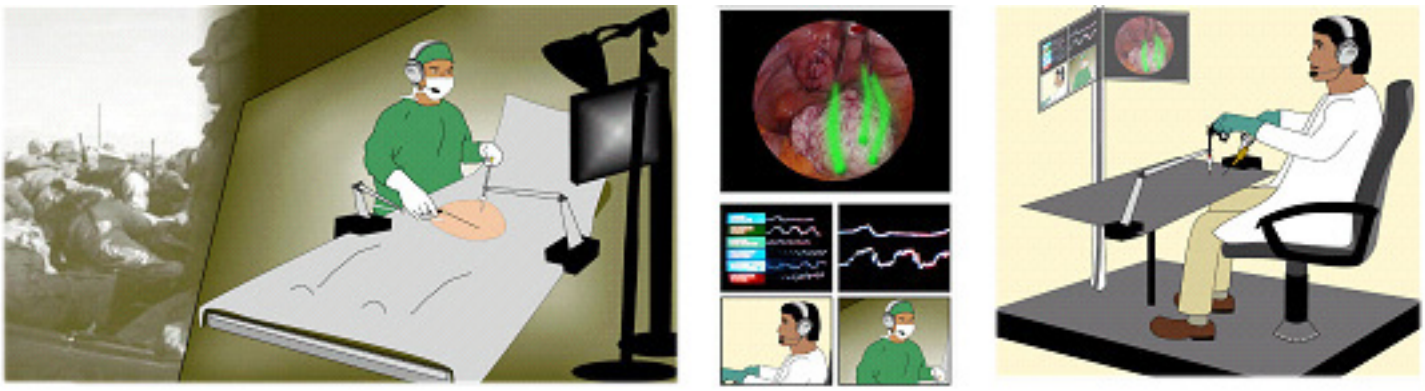
- 110 Journal and Conference Publications
- 8 Projects
- 6 Key Technologies
- 18 Collaborations

CASIT has also partnered with Intuitive Surgical, Karl Storz Endoscopy, Metronics, US Surgical, Ethicon, Siemens, Berchtol, Jet Propulsion Laboratory (JPL), Institute for Pure and Applied Mathematics (IPAM), UC Santa Barbara (UCSB) Department of Electrical and Computer Engineering, Brown Research Group at UCSB, Rehabilitation Medicine Department and Gonda Vascular Center at UCLA, UCLA Center for International Medicine (CIM), NMCSD, and NHRC.

CASIT brings together a extensive multidisciplinary team of physicians, scientists, and engineers. This resource, and the addition of the new hospital, provides the organization with a unique and powerful opportunity to develop research programs that will improve surgical quality, safety, efficiency, training, and develop new interventional surgical techniques.

Telementoring System for Laparoscopy

The CASIT team has developed and is testing a device to help train novice laparoscopic surgeons through the use of telementoring and haptic control. This system allows a novice surgeon to freely conduct a laparoscopic procedure, receiving assistance (when needed) from a skilled surgeon via actuator control feedback (haptic feedback) of the laparoscopic tools and through intraoperative videoconferencing. The novice surgeon can learn the motions and forces a skilled laparoscopic surgeon uses to perform specific tasks within the surgery through the haptic feedback. The telementoring aspect also allows the skilled surgeon to be located in another room or another country; thus, allowing for remote access to skilled laparoscopic surgeons in areas that



In the development of a haptic guidance system to facilitate minimally invasive surgical training and telementoring, an expert surgeon's motions are recorded during a procedure (left). This data is used to develop a training simulation where novice surgeons practice by imitating the expert surgeon's gestures (right).

would not previously have had such an asset (i.e., rural areas to forward deployed medical facilities).

Implementation of the concept was achieved through the integration of low-profile actuators and sensors into traditional laparoscopic instruments on both the novice and skilled surgeon's tools. The sensors provide special information of each tool. The actuators integrated into the system allow a skilled surgeon to remotely use the instruments without physically touching the tools in the OR.

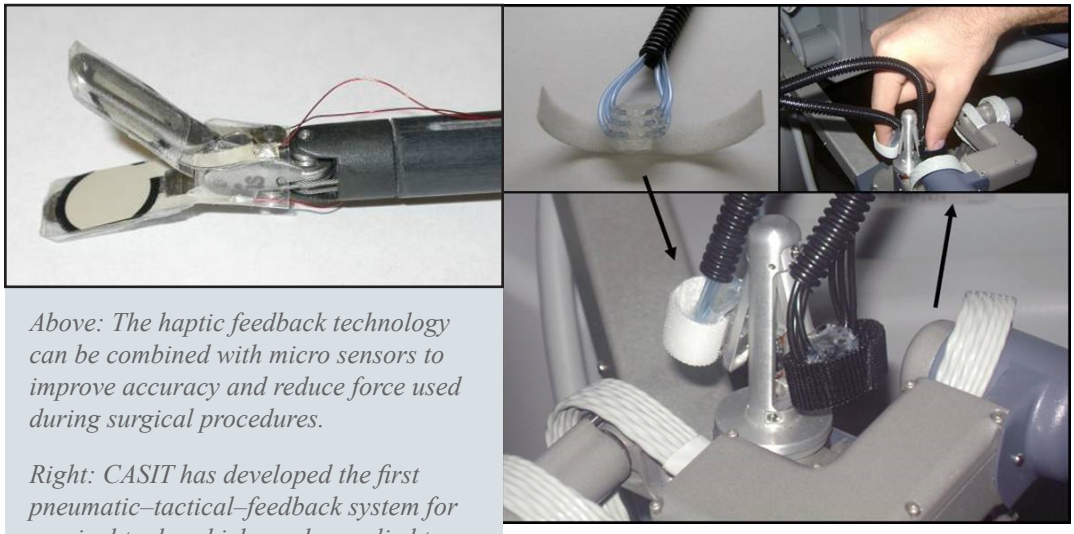
Pneumatic Haptics for Robotic Surgeons

Robot-assisted minimally invasive surgery offers improved range of motion over standard laparoscopic techniques, but is characterized by a total loss of haptic feedback, requiring surgeons to rely solely on visual cues. Visual information is sufficient for many procedures; however, it is often challenging to characterize tissues and apply appropriate forces to sutures without tactile information. Tactile feedback may also enable expansion of robotic surgery to other surgical procedures that are difficult to perform without a sense of touch.

The development of a pneumatic balloon-based tactile feedback system is currently underway at CASIT. Forces are detected at the distal end of the robotic grasper via a force sensor array, and the forces from each sensor element are translated to proportional pressures that are applied to the surgeon's fingers via balloon actuator arrays. This system is currently under development for use with the Da Vinci robotic surgical system. A reduction in grasping force has already been demonstrated using the system.

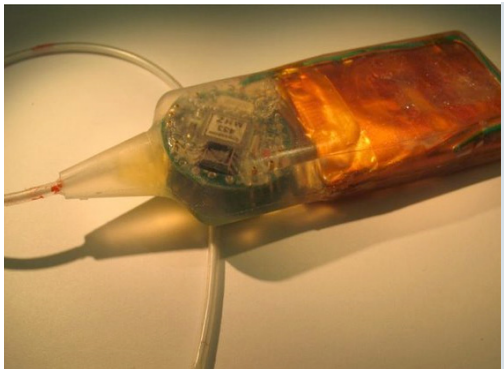
MEMS Sensors for Continuous Physiological Monitoring

CASIT is developing an implantable sensor network for biomedical applications based on distributed network technology and *in vivo* sensors. This system has three components: 1) the miniaturized sensor module contains various physical and chemical MEMS sensors in a biocompatible package; 2)



Above: The haptic feedback technology can be combined with micro sensors to improve accuracy and reduce force used during surgical procedures.

Right: CASIT has developed the first pneumatic–tactical–feedback system for surgical tools, which can be applied to both robotic and laparoscopic devices.



MEMS technology has been used to create miniature pressure sensors that can be implanted into the body. The current application is for measuring bladder pressures, allowing for non-invasive assessment of bladder function. As the technology is miniaturized, multiple additional applications in the brain, heart, and GI track are possible.

a sensor node contains the power supply, signal conditioning circuit and wireless transceiver, and 3) a PDA provides the communication hub where physiological data is managed, stored, and displayed. Individually, each sensor module can record critical vital signs and physiological parameters of the monitored system. Together, the distributed sensor network acts as a collective monitor of systemic symptoms. Based on the CASIT database, it can assess valuable interrelated effects of physiological profiles under specific perturbations never before possible.

The first generation of this concept is a minimally invasive implantable pressure sensing system to assess the gross pressure change in the bladder and renal pelvis. The sensor module can be adapted for other types of physiological sensors.

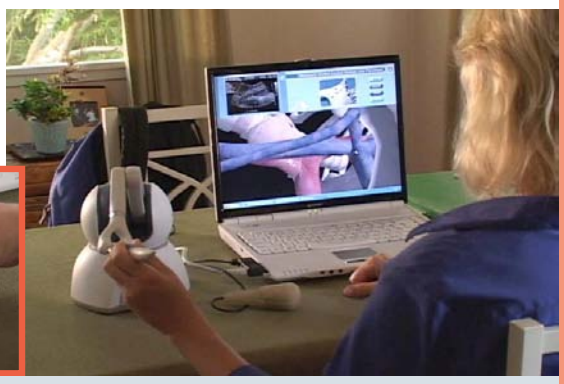
Robotic Telepresence for Subspecialty Care

A software application for remote wireless access in real time to a comprehensive set of medical data is being developed. A wireless mobile pocket device will allow access to all data, including viewing radiographic imaging connected to the picture archiving and communication systems (PACS) system. The entire medical electronic record can be accessed remotely in real time. New high-speed cell phone networks are employed. This technology will be fused with the InTouch robot for virtual physician presence at the bedside, in the Emergency Room, or on the battlefield. It will allow for remote expert consultation, with the ability to view the patient, interview the patient, and assess a complete set of medical data in real time.

Advanced information technology allows for improved communication between the doctor and patient.

Procedure Simulation

Computer-based procedural training and educational methods are being explored to practice procedures without risking iatrogenic injury. The project continues to develop a desktop computer-based platform that will train users how to perform ultrasound-guided procedures. This system will provide a platform for the development of additional procedural training using text, audio, digital video, 3D modeling, and force feedback.

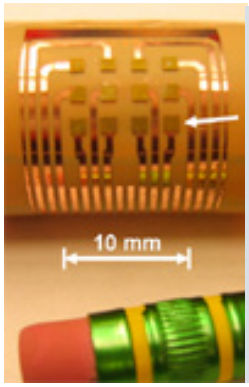


Advanced medical simulation and training techniques allow students to learn technical skills using simulated images for training purposes.

Conformable Array Ultrasound

The ability to accurately and rapidly diagnosis fractures, shrapnel, wound tracts, and soft tissue injuries are key to effective rapid treatment. Traditional radiographic methods require heavy, bulky x-ray systems that are not suitable for far forward bases or in the

field. Current ultrasound systems have shown great promise for diagnosis in the field, but the skills needed for operation and manipulation of the transducer and lack of volumetric data often limit their effectiveness.



Traditional ultrasound probes use rigid arrays to obtain images. CASIT has developed flexible, comfortable, ultrasound arrays which conform to the body's surfaces and develop 3D images.

CASIT's preliminary evidence suggests that flexible conformable ultrasound arrays for medical imaging are feasible and applicable to the problem of fractures and vascular injuries in arms, legs, head and neck, as well as detection of shrapnel and wound tracts. These arrays have the advantage of providing multiple unique "looks" around objects and can produce high resolution volumetric images of human extremities in real time. This blood-pressure cuff-type flexible conformable array will allow less experienced personnel to obtain high quality images with minimal manipulation of the affected extremities, since mechanical scanning is not required. These arrays offer the additional advantages of lower power consumption, high portability (laptop), and durability for battlefield use.

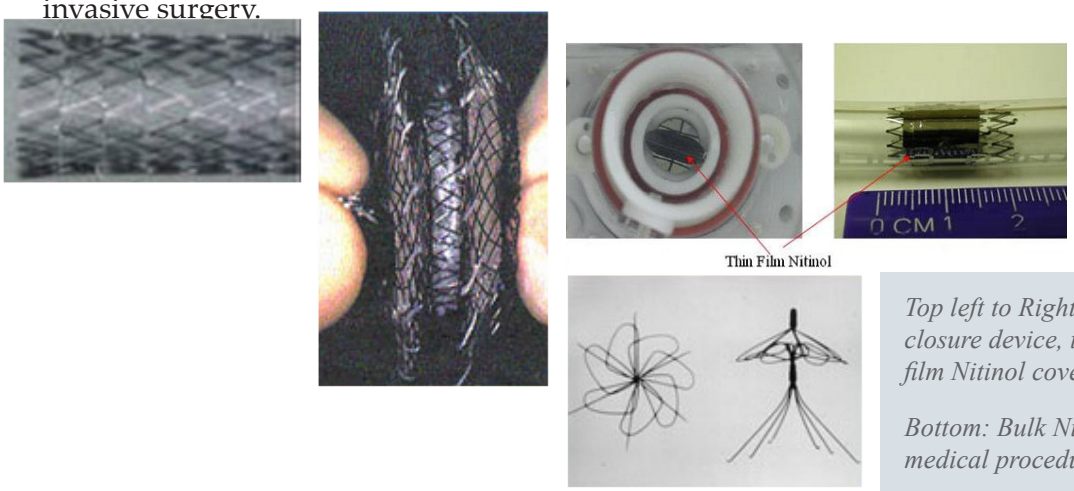
This research project is part of an ongoing collaboration between CASIT and the UCSB Department of Electrical and Computer Engineering, the UCLA Department of Bioengineering, and the UCLA Department of Surgery. This group has previously developed acoustic modeling tools using finite element simulations, transducer fabrication techniques, signal processing algorithms, and testing and characterization methods for various ultrasound applications, ranging from dental ultrasound to minimally invasive surgery.

Thin-film Nitinol Devices for Vascular Repair

Rapid and minimally invasive controls are needed to prevent excessive hemorrhaging from major arteries in wounded Warfighters on the battlefield or in civilians appearing at urgent care facilities with significant trauma. The focus of this research is to develop an ultra-low profile device containing new thin film Nitinol to occlude the damaged vessels preventing excessive blood loss, as well as subsequent repair.

Nitinol is an excellent biocompatible, equiatomic alloy with many desirable attributes ideal for vascular repair. Bulk Nitinol has been used in transcatheter applications in many currently available medical devices; however, the delivery systems for bulk Nitinol are relatively large compared to thin film due to the material's physical dimensions. Thin film Nitinol (i.e., less than $\frac{1}{5}^{th}$ the diameter of a human hair), is ideal for patching vascular damage or occluding blood flow. The thin film Nitinol also dramatically reduces catheter sizes while presenting an ideal opportunity to develop new ultra-low profile vascular repair devices.

During the last two years UCLA has studied the use of thin film Nitinol in several related devices, including heart valves and covered stents. The work at CASIT builds upon these advancements to develop several new ultra-low profile vascular repair devices.



Top left to Right: A Bulk Nitinol stent, Bulk Nitinol ASD closure device, thin film Nitinol heart valve, and a thin film Nitinol covered stent developed and built at UCLA.

Bottom: Bulk Nitinol vena cava filter used in current medical procedures.

Pneumatic Haptics for Prostheses

A novel pneumatically driven balloon-based tactile feedback system is currently under development for lower-limb amputees and for patients with lower-limb sensory neuropathy. The system will translate the pressure distribution on the feet into tactile information which can in turn be relayed to the body through a series of balloon actuators. For lower-limb prosthetic patients, the system can provide tactile information from the prosthetic foot to the residual limb of the amputee, potentially shortening the learning curve of balance in standing and gait during the training phase of the rehabilitation. Patients with lower-limb sensory neuropathy would also benefit from this technology by regaining balance and gait faster, and also by preventing accidental injuries which may lead to amputation.

A prototype haptic feedback system has already been developed, and preliminary tests have demonstrated that healthy subjects can distinguish the location and magnitude of stimuli on the upper leg with accuracy greater than 90%. Development and clinical testing of the device is being performed at CASIT in collaboration with Rehabilitation Medicine Department and Gonda Vascular Center at UCLA, with the NMCSD, and the NHRC. This material is based upon work supported by the National Science Foundation (NSF).

CASIT Representative Publications

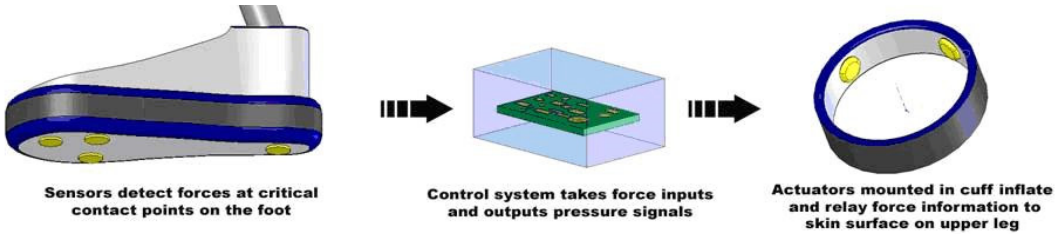
King CH, Culjat MO, Franco ML, Lewis CE, Dutson EP, Grundfest WS, Bisley JW, "Tactile feedback induces reduced grasping force in robotic surgery. " *IEEE Transactions on Haptics*. 2009; 2: 103-110.

Culjat MO, Bennett DB, Lee M, Brown ER, Lee H, Grundfest WS, Singh RS, "Polyimide-based conformal ultrasound transducer array for needle guidance." *IEEE Sensors Journal*. 2009; 9: 1244-1245.

Fan RE, Wottawa C, Boryk RJ, Sander TC, Wyatt MP, Grundfest WS, Culjat MO, "Pilot testing of a tactile feedback rehabilitation system on a lower-limb amputee," *Proceedings of 2009 ICME/IEEE International Conference on Complex Medical Engineering.* DOI 10.1109/ICCME. 2009; 4906337 pp 1-5.

Chun Y, Levi DS, Mohanchandra KP, Vinuela F, Carman GP, "Thin Film Nitinol Microstent for Aneurysm Occlusion," *J. Biomech Eng.* 2009; 131: 051014.

King CH, Culjat MO, Franco ML, Bisley JW, Carman GP, Dutson EP, Grundfest WS, "A multi-element tactile feedback system for robot-assisted minimally invasive surgery," *IEEE Transactions on Haptics*. 2009; 2(1): 52-56.



Using the haptic feedback technology, developed for surgical tools, CASIT has designed and tested a technology that can return sensation to amputees and patients with lower limb neuralgic deficits. This technology appears to improve gait and decrease the rehabilitation time for patients with amputation or stroke.

The Center for Integration of Medicine and Innovative Technology (CIMIT)

www.cimit.org

A Model Process for Stimulating Medical Technology Innovation

CIMIT is a founding partner of TATRC, with both organizations evolving together since their inceptions more than a decade ago. Dr. John Parrish was recognized this year for his leadership of CIMIT and his extraordinary contribution to DoD programs (see Awards and Recognitions). The CIMIT model of active partnering and mentoring of engineering and medical science projects has gained national and international attention as a model for other research funding organizations. In 2007, it was the subject of a detailed review and analysis by the Harvard Business School. CIMIT's focused approach to improving patient care is based on facilitated collaboration among scientists, engineers, and clinicians to catalyze the discovery, development and implementation of innovative technologies, emphasizing minimally invasive approaches. This is accomplished through a non-profit consortium of Boston teaching hospitals and engineering schools.

- Massachusetts General Hospital
- Brigham and Women's Hospital
- Massachusetts Institute of Technology
- Charles Stark Draper Laboratory
- Beth Israel Deaconess Medical Center
- Boston Medical Center
- Boston University
- Children's Hospital Boston
- Harvard Medical School
- Newton-Wellesley Hospital
- Partners HealthCare
- VA Boston Healthcare System

CIMIT's core portfolios of multi-disciplinary, inter-institutional research projects are led by a diverse group of subject matter experts in emerging areas of medical innovation. Additional individuals act as "site miners" for their respective institutions, identifying and connecting potential research collaborators across disciplines and institutions.

Representative CIMIT 2009 Successes

Novel, Non-Invasive, Patient-Specific Electrographic Seizure Warning System

CIMIT is building and evaluating a non-invasive, patient-specific system that accurately detects electrographic seizure onset sufficiently in advance of the onset of clinical symptoms to warn the patient of an impending seizure or automatically trigger potentially abortive therapy. This detection system is capable of learning to recognize seizure onset patterns with high sensitivity and specificity. CIMIT aims to integrate this automated seizure detection system with an audible alarm and the Vagus Nerve Stimulator (VNS), to trigger acute VNS stimulation as an acute abortive therapy upon seizure detection. The audible alarm could potentially ameliorate the consequences of seizures by giving patients and caregivers time to seek a safe position or to admin-

CIMIT FAST FACTS FY98 - FY09

Basic products	
▪ Publications	500+
▪ Invention disclosures	200+
▪ Patents issued	30+
Technology Transfer	
▪ Technology licenses	10+
▪ Companies formed	20+
▪ Industry partnerships	40+
▪ CIMIT-supported devices introduced into patient care	14+
▪ Projects in clinical trials	17

▪ A detailed analysis of CIMIT's "return on investment" is currently underway and will help to serve as a model for a similar effort at TATRC.

Seizure onset detection system, control computer, and VNS.

ister an acute pharmacological therapy. Results to date include the development and integration of the system with VNS as well as the successful demonstration in five patients in a clinical setting (VA Hospital).

Transcranial Near-Infrared (NIR) Light for TBI

NIR can penetrate the skull and reach into the brain. The effect of this light is to prevent brain cells dying, increase cellular energy, and reduce inflammation and swelling. These beneficial effects are exactly what are needed to reduce the escalating brain damage that occurs after head injury. This project is studying the effects of NIR on brain cells in culture and measuring the beneficial effects of the therapy in mice that have been subjected to controlled head injuries. If successful, this treatment would likely be rapidly adopted in both military and civilian medicine. Preliminary results suggest that low-level laser therapy reduces brain damage after closed-head TBI and also improves learning and memory.

Combat Medic Training System (COMETS)

The purpose of this research is to design, fabricate, and conduct field testing of a completely autonomous highly-realistic prototype casualty simulator that is able to withstand harsh field conditions and decontamination during combat trauma and CBRNE exercises. Emphasis is to be placed on durability, ease-of-use, and cost effectiveness resulting in a system that exceeds stated military objectives for the next generation of casualty simulators. A prototype has been developed and field tests are planned for the future.

A simulation excercise with COMETS.

CIMIT Portfolios and Leaders

Biodetection & Sepsis Control
Jeffrey A. Gelfand, MD, FACP

Biomaterials & Tissue Engineering
Jeffrey Borenstein, PhD

Cardiovascular Disease
Thomas Brady, MD

Clinical Systems Innovation
David Judge, MD

Global Health Initiative
Kristian Olson, MD, MPH, DTM&H

Image Guided Therapy
Ferenc Jolesz, MD

Inhalation Technology
Augustine MK Choi,

Minimally Invasive Surgery
David Rattner, MD

Neurotechnology
Steven Schachter, MD

New Initiatives
Kirby G. Vosburgh, PhD

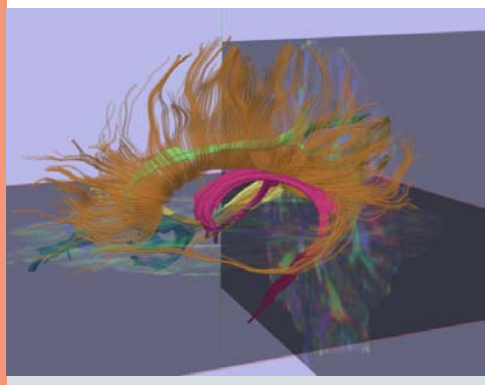
Optical Diagnostics
Gary Tearney, MD, PhD

Post-Traumatic Stress Disorder (PTSD)
Roger Pitman, MD

Simulation
Steve Dawson, MD

Trauma & Casualty Care
George Velmahos, MD, PhD

Traumatic Brain Injury (TBI) & Neurotrauma
Ross D. Zafonte, DO



Some of the major white matter fiber bundles identified through DTI.

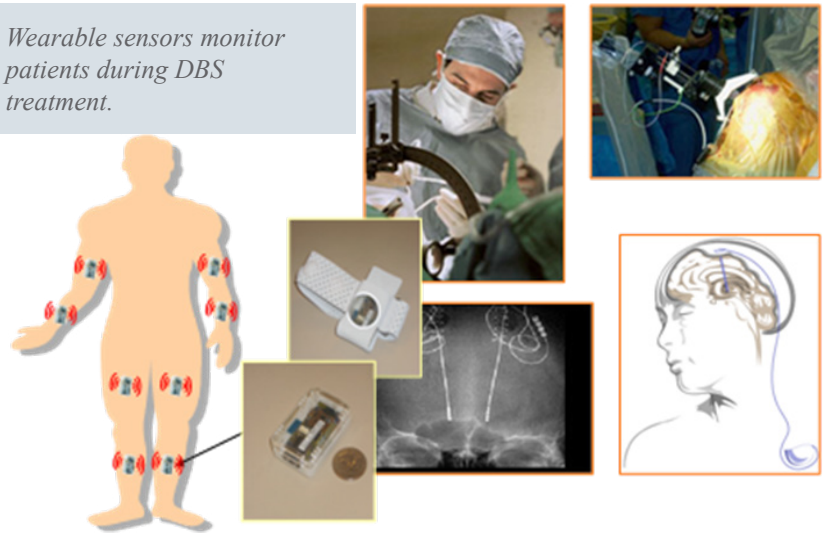
More Sensitive Brain Imaging Technique

The most common form of TBI includes Diffuse Axonal Injury (DAI). Currently, conventional imaging techniques are not likely to diagnose DAI, because these methods are not sensitive to subtle white matter pathology. Recent studies have shown that Diffusion Weighted MRI and Diffusion Tensor imaging (DTI) are able to quantify DAI compared with other imaging modalities. CIMIT has conducted a small clinical trial at a VA Hospital, with plans for larger comprehensive trials

Wearable Sensors to Monitor Patients During Deep Brain Stimulation (DBS) for Improved Motor Control

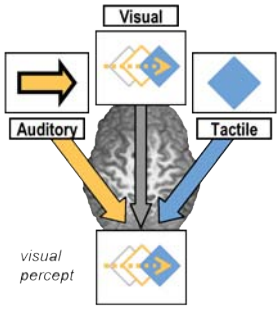
A significant percentage of Parkinson's Disease (PD) patients have motor control deficits. Deep Brain Stimulation (DBS) helps some patients, but clinical improvements are delayed and difficult to quantify. CIMIT's solution is to develop wearable sensors and data analysis techniques to monitor patients during DBS treatment. Future plans include a system for remote monitoring in the home and to explore the use for treatment to increase motor control in PD.

Wearable sensors monitor patients during DBS treatment.



Multi-modal Sensory Rehabilitative Strategy for the Augmentation of Functional Vision

Eye injuries for the Warfighter are increasing. The development of sensory substitution devices and visual prostheses require a better understanding of how the brain adapts to blindness. CIMIT investigators are developing an integrated multi-modal sensory platform for visually impaired patients using tactile and auditory information to enhance object recognition skills. A prototype for a cross-modal sensory interface has been built and is now being tested.



Audio-spatial cues and haptic exploration of the environment generates a robust immersive experience for the blind user, and stimulates functional recruitment of the visual cortex.

Huperzine to Reduce to Prevent TBI and Seizures

Huperzine A is widely used to treat Alzheimer's Disease and other memory disorders. This therapy could be used prophylactically for individuals at high risk for TBI. Preliminary studies have found Huperzine A to be effective in pre-human models for treating pain and seizures. CIMIT is investigating the safety and efficacy of Huperzine A for persons at risk for TBI or post-TBI.

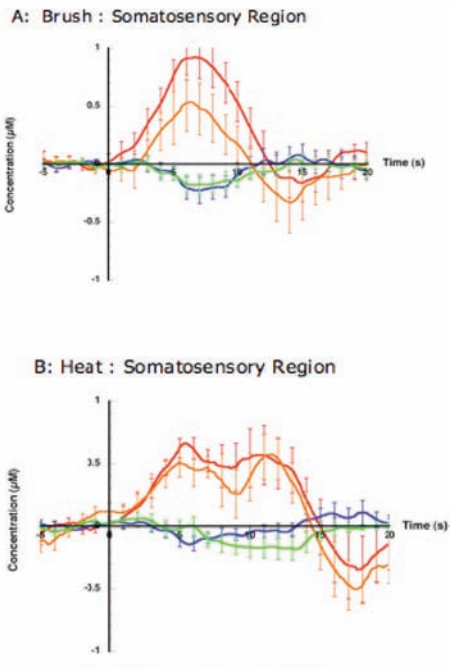
SmartPad: Electrocardiogram (ECG) Monitoring During Transport

Patient on a SmartPad, and the resulting ECG.

Trauma patients require continuous monitoring during transport (ECG, respiration, blood oxygenation). Traditional ECG monitoring includes use of adherent pads and wires, which often loosen or become dislodged, resulting in inaccurate measures. CIMIT's solution has been to eliminate the sticky pads and cables and create a silastic sensor placed on a stretcher using off-the-shelf materials. It uses electrode arrays as embedded sensors to monitor ECG and automatically scans to find the optimal signal. The system is able to acquire ECG signals for different body orientations and battery powered wireless results in lower noise in ECG signal. This results in continuous cardiac monitoring solution for trauma (in hospital or in disaster settings) and provides a wireless link to a laptop.

Near-Infrared Spectroscopy (NIRS) to Evaluate Pain and Consciousness

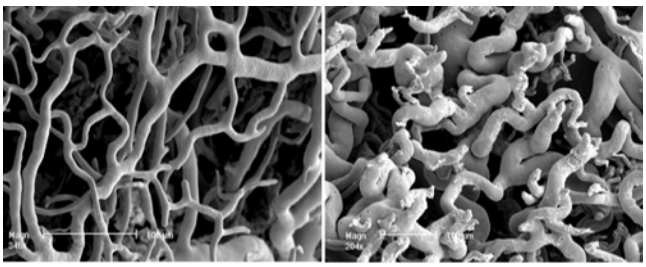
Patient awareness and pain during anesthesia or sedation carries significant consequences, including post-traumatic stress disorder (PTSD), with no current objectives measures. CIMIT's solution detects cortical activity associated with pain and consciousness by using Near-Infrared Spectroscopy (NIRS). This non-invasive, real-time evaluation of pain and consciousness poses great utility in potentially mitigating the incidence of surgical-related PTSD, as well as monitoring pain in our wounded Warriors, particularly those who cannot communicate and those in pediatrics.



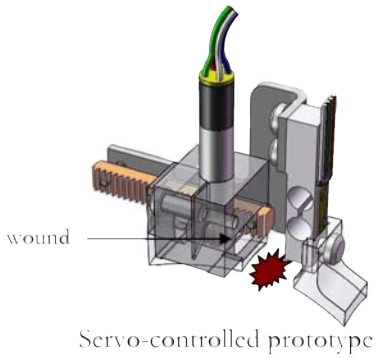
Non-pain (Brush) vs. painful (Heat) responses.

Use of Micro-Mechanical Forces to Accelerate Wound Healing

Many injured Warriors experience debilitation due to chronic non-healing wounds. An increase in the incidence of chronic wounds due to aging population and type II diabetes also results in significant disabilities with tremendous cost. Basic science observations show powerful stimulatory effects of external mechanical forces on cellular proliferation. CIMIT is developing and testing a micromechanical force device that accelerates wound healing. To date, a second generation servo-controlled prototype has been developed and clinical studies have been conducted on abdominal wounds, chest wounds, and pressure sores.



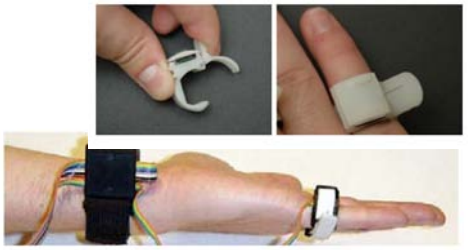
The baseline (left) wound with poor vasculature, as compared to the same wound (right) with continuous force applied, which promotes enhanced vascularity.



Servo-controlled prototype

Wearable "Imperceptible" Medical Sensors

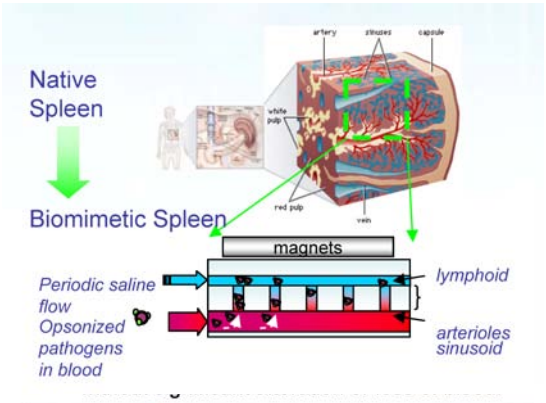
Blood pressure monitoring can reveal if medication is appropriate, if a wounded Warfighter is bleeding, or if an elder living at home alone is experiencing a medical emergency. Standard blood pressure cuffs are not appropriate for long-term use; however, CIMIT is developing unobtrusive sensors which and can be fitted into a ring or a sleeve and can be worn long-term. To date, prototypes have been developed and validated during laboratory tests. DoD provided the initial funding for this research; subsequent funding has come from NIH, NSF, and private industry.

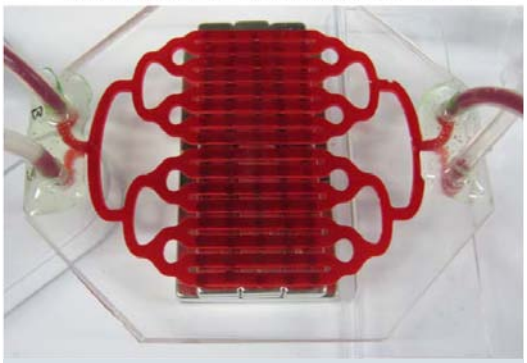


Examples of wearable medical sensors include a clip-on sensor for wounded Warfighters or civilians, and a new blood-pressure sensor that uses pure light and no squeezing cuff.

Nanomagnetic Microfluidic Separator for Sepsis Control (Artificial Spleen)

Fungal infection sepsis causes 200,000 deaths/year in the US. The overall death rate is 25% in the US and is significantly higher for Service Members and for the international population. CIMIT is developing an extracorporeal device that rapidly (1 to 4 hours) clears 90-99% of pathogen load. The first generation device removes 80% of fungi from whole human blood, while the second generation device is more robust and simpler to manufacture.



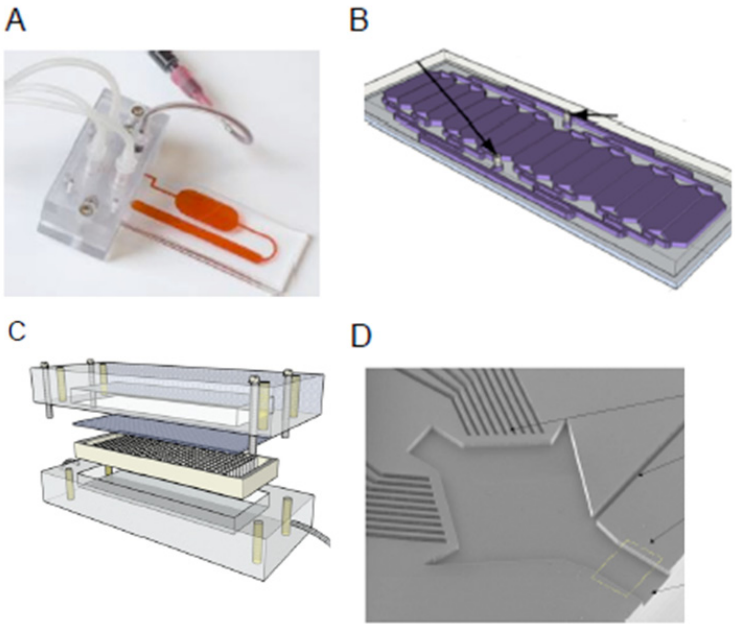


A biomimetic spleen replicates native structure and function of organ to remove pathogens without altering blood. The prototype biomimetic spleen shown here has 16 parallel channels which remove nearly all opsonized pathogens without significant alteration or loss of blood.

A Microfluidic System for Monitoring Sepsis at the Point of Care

Sepsis is a systemic response to an infection that can be bacterial, viral, fungal or parasitic in origin. Current standard of care relies on diagnosis based on the patient's history and presentation. Blood cultures are taken, but the results can take days to complete. Treatment is based on symptoms and broad-spectrum antimicrobials are given immediately. Specific treatment of the infectious agent is only possible after the blood cultures are complete. Since sepsis is such a rapid onset condition, the initial resuscitation and management of a septic patient are almost always done in the absence of knowledge of the type of infection. Current FDA approved "rapid" diagnostic tests can identify sepsis with reasonable sensitivity and specificity, but not the causative organism.

Tests aimed at pinpointing the infectious agent, like the Roche SeptiFast tests, approved for use in Europe, rely on large numbers of polymerase chain reaction (PCR) assays specific to each organism and take six hours to complete. The Klapperich Laboratory is developing and testing a rapid, point-of-care test to monitor sepsis that quantifies the amount of circulating free and cell/infectious agent associated nucleic acids in blood. The test show the clinician if the infection is bacterial or fungal; and if bacterial, is it gram-positive or gram-negative? This test is based on technology that allows fast and efficient extraction of nucleic acids from complex biological samples, including blood. Collection of a purified, concentrated sample of nucleic acid from whole blood takes less than 10 minutes to perform in our prototype device, and with the addition of a PCR module for detection, we aim to complete the entire assay in less than one hour.



Microfabricated devices and assemblies for (a) CD4 counting; (b) leukocyte RNA isolation; (c) cancer diognostics; and (d) the study of cell migration in the response to a chemotactic gradient.

A Label-Free Viral Detection Microchip for Point-of-Care Applications

Efforts to develop point-of-care viral assays by miniaturizing "PCR on a chip" have not yet succeeded. Dr. Mehmet Toner's lab is developing a point-of-care, viral measurement microchip based on mass sensing. The final system will integrate three technologies: nanofiltration, inertial particle focusing in a microfluidic channel, and mass sensing using a suspended nanochannel resonator, with piezoresistive readout—to create a prototype device that can measure virion mass directly from whole blood. By direct measurement of viral particles, the system will avoid the problems associated with sample preparation and amplification that make current methods of viral detection challenging to implement for point-of-care systems. The the most pressing need for point-of-care viral detection, in the US and globally, is in HIV disease, and the focus will be on HIV viral load measurement. This can be extended to influenza, avian influenza, hepatitis, cytomegalovirus, dengue, and bioterror pathogens.

CIMIT Representative Publications

Ryou M., et al. NOTES Thoracic Surgery in a Human Cadaveric Model: Transesophageal Exploration of the Mediastinal, Pericardial and Pleural Spaces Followed by Pleural Biopsy, Lymph Node Sampling, Thoracic Duct Ligation, Vagotomy, Thymectomy and Pericardial Window. *Gastrointestinal Endoscopy* 2009; 67: AB111.

Becerra L, Harris W, Grant M, George E, Boas D, Borsook D. Diffuse optical tomography activation in the somatosensory cortex: specific activation by painful vs. non-painful thermal stimuli. *PLoS ONE*. 2009; 4: e8016.

Arney D, Fischmeister S, Goldman JM, Lee I, Trausmuth R. Plug-and-Play for medical devices: experiences from a case study. *Biomed Instrumentation Technol*. 2009; 43: 313-317.

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Rullmann M, Anwander A, Dannhauer M, Warfield SK, Duffy FH, Wolters CH. EEG source analysis of epileptiform activity using a 1 mm anisotropic hexahedra finite element head model. *Neuroimage* 2009; 44: 399-410.

Hawaii Federal Health Care Network (HFHCN)

www.pacifichui.org

Cultivating Biotechnology for DoD Medical Advanced Technology

Biotechnology currently represents but a small sector of the Hawaii workforce, but Hawaii is uniquely positioned to succeed in key sectors of this competitive industry. Although Hawaii makes up only 0.4% of the US population, some projections indicate that Hawaii's biotech industry will generate $3.1 billion in revenues by year 2010 — 2.3% of the US total. The state is home to hundreds of trained researchers with expertise in agricultural, medical, and marine research. Furthermore, science and technology R&D in Hawaii is supported through a number of agencies, including the High Technology Development Corporation, the Maui Research & Technology Center, the Natural Energy Laboratory of Hawaii Authority, Center of Excellence in Ocean Sciences, Pacific Center for High Technology Research, and the Hawaii Natural Energy Institute.

Other prominent research centers include Hawaii Biotech, Inc. (HBI), which integrates genetics, engineering, immunology, and chemistry to address major unmet human health needs in the areas of infectious disease, inflammation, cancer, and drug discovery. HBI has received research funding from the National Institutes of Health (NIH), TATRC, and other state and federal institutions, and is now moving into efficacy testing of vaccines for West Nile Virus and dengue, among others.

Cellular Bioengineering, Inc. (CBI) is another Hawaii-based accelerator of technologies with biomedical and biodefense applications. With TATRC funding and other federal and private support, CBI has developed and tested a bio-integrating polymer corneal substitute which restores sight to people in need of corneal transplant. CBI has also developed a bio-sensor using cardiac cells growing on a digital computer chip that can provide early detection of chemical or biological threats.

Many of the other companies highlighted in this report are either small Hawaii-based companies whose founders recognized the many advantages attached to the island state, or those that have moved operations to Hawaii to take advantage of climate, tax advantages, R&D infrastructure, and social capital.

A Pacific Rim Research Hub

Hawaii's strategic location in the Pacific Rim and its life science centers makes it a logical partner in the global marketplace of biotechnology research, product development, and services. Hawaii is an ideal location for life science firms from Asia to establish a research presence in US biotechnology research.

One example of the strategic use of Hawaii's location is the "Advanced Technologies Addressing Asia-Pacific Infectious Diseases," a TATRC-funded project. The University of Hawaii is developing a pilot zoonotic disease detection program in the Asia-Pacific Region which involves expanding the active surveillance system to provincial and district hospitals in VietNam and the training of laboratory staff there. This program is designed to provide an important early warning disease detection system for both known and unknown pathogens that have epidemic potential.

Several other TATRC-sponsored projects involve Pacific Rim involvement. Building upon previous evaluation work, TATRC funding has effected deployment of remote ICUs to Tripler Army Medical Center (TAMC), Guam Naval Hospital (USGNH), and Brian Allgood Army Community Hospital (BAACH) in Korea. The program enables TAMC specialists to participate in remote crisis team training, manikin-based simulation, and provide care to ICU patients at USGNH and BAACH.

HFHCN FAST FACTS FY05 - FY09

- 24 Active Projects in 2009
- 20 PIs FY06 - FY09
- $65M+ Funding

Hawaii Vendor Industry Day

The HFHCN sponsored a Hawaii Vendor Industry Day in November 2009, that included attendees from academia, industry, and the military. The one-day conference, held in Honolulu, HI was intended to educate and assist Hawaii-based companies competing for DoD research and development funds. Ms. Jennifer Sabas, Chief of Staff for US Senator Daniel Inouye (D-HI), provided the opening remarks on behalf of the Senator. Dr. Terry Rauch from Health Affairs, Force Health Protection and Readiness, discussed the Defense Medical Research and Development Program's investment and execution priorities. Other representatives from DoD and USAMRMC included COLs Jeff Unger and Karl Friedl. Ms Jeannie Shinbur provided information on DoD areas of interest, funding opportunities, transition to advanced development, and contracting.

Recent HFHCN Accomplishments

Advanced Technologies Addressing Asia-Pacific Infectious Disease

Mentioned previously, this important early warning disease detection system for both known and unknown pathogens that have epidemic potential will benefit civilian populations and national security planners, in addition to the described Warfighter and public health benefits.

Rapid Adverse Identifier for Drugs and Evaluation Resource (RAIDER)

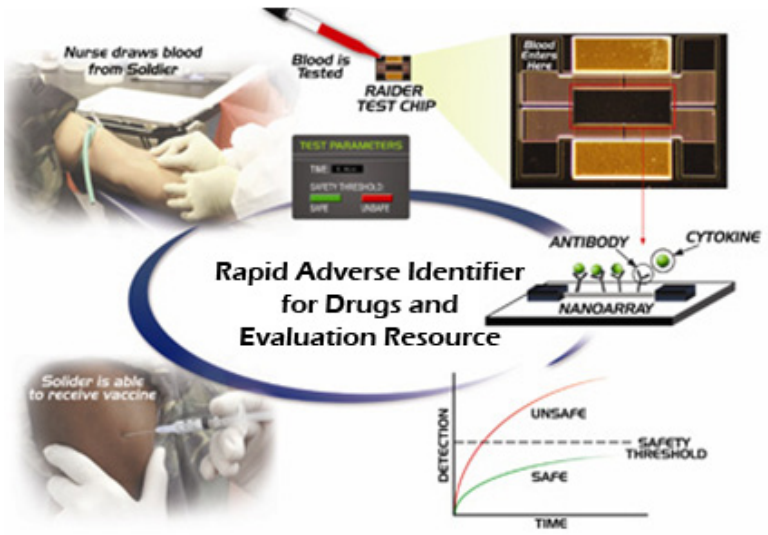
Oceanit Laboratories has developed a nanobiosensor chip-based system that can predict adverse drug reactions (ADRs) at the point-of-care level; thereby, preventing serious ADRs due to drug or vaccine administration. The Rapid Adverse Identifier for Drugs and Evaluation Resource (RAIDER) platform is composed of a silicon carbide handle grafted with vertically aligned carbon nanotubes, yielding a nanoarray configuration. Current funding will assess the technical feasibility of creating a unique nanostructure that can be functionalized to serve as a target capture, and optimize in a nanobiosensor to detect histamine and certain cytokines involved in hypersensitivity immune reactions.

Development of Technologies for Bioengineered Tissue Repair

Cellular Bioengineering Inc. is pioneering therapies for improving and restoring vision by developing biosynthetic substitutes for corneas that have been injured as a result of injury or disease. TATRC funding has supported both the culture and transplantation of endothelial cells on corneal substrates, and the development of a bio-integrating polymer. CBI's synthetic biopolymer is currently being tested in a 10-patient corneal transplant pilot study in Europe, for which preliminary results show no rejection or extrusion. Advancement of this technology promises to address virtually all types of corneal blindness and, without the need for a human donor, represents a significant benefit to Warfighters being treated in military medical facilities.

Pacific Pediatric Advancement Care Initiative

A broadly collaborative group, including the University of Hawaii (UH), TAMC, the University of Pittsburgh Medical Center (UPMC) and the Kapiolani Women's and Children's Medical Center (KWCMC), is working to establish a new extracorporeal life support (ECLS) program which employs use of extracorporeal membrane oxygenation (ECMO).

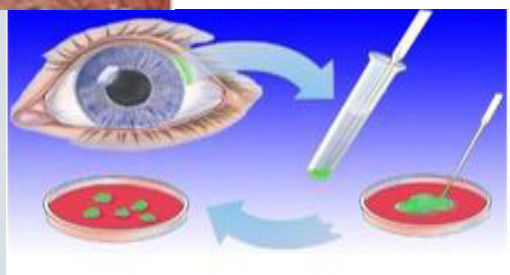


By providing a simple method to predict Type I hypersensitivity reactions to vaccines or drugs, RAIDER serves as an enabling technology to help prevent casualties of biological warfare. The real-time monitoring capabilities of the RAIDER technology make it ideal for field and point-of-care use.

The project examines the use of ECMO in endotoxin-induced septic shock, use of blood substitutes in place of whole blood as a heart-lung machine priming substitute, and the effect of ECMO in multisystem organ failure related to septic shock. The effort also seeks to create a unique ECLS training curriculum that integrates the use of manikin simulation for training, testing, and evaluation.

Treatment of Peripheral Vascular Disease by Adipose-derived Stromal Cell Injection

CBI is exploring biosynthetic therapies for improving and/or restoring vision to the cornea as a result of battle-related eye injury or disease.



Tissue Genesis, Inc.'s (TGI) current work is advancing regenerative medicine to enhance recovery after battlefield injuries. This project is investigating whether Adipose-derived stromal cells (ASCs) can be delivered directly to ischemic tissue by intramuscular injection into ischemic tissues or through *in situ* vasculature and to increase distal circulation and relieve the symptoms of peripheral vascular disease. TGI has successfully developed a portable, automated cell separation system and patented process that isolates and sorts human fat tissue into therapeutic cells.

Intelligent PTSD Classification and Treatment-Augmentation Technology

Archinoetics is using infrared biosensors to improve the diagnosis of PTSD. The "Intelligent PTSD Classification and Treatment-Augmentation Technology" project will develop, implement, and validate a technological solution to existing diagnostic difficulties. The significance of this effort is that it will offer a more efficient alternative to current diagnostic strategies for PTSD. As it will also provide the capability of real-time continuous monitoring of autonomic nervous system activation, it can subsequently be used as a telemedicine treatment modality.

Accelerated Optimization of Small Molecule Inhibitors of *Botulinum A* Light Chain

PanThera Biopharma is expanding drug discovery efforts to produce a safe and effective small molecule drug that can be used to treat Botulinum neurotoxin serotype (BoNT/A) poisoning. Using an empirically derived Botulinum neurotoxin serotype (BoNT/A) Accelerated Screening Cascade (ASC) to guide inhibitor optimization, PanThera is currently testing successful lead compounds in a mouse survival model. The intended therapeutic product will be effective against post-exposure intoxication, and provide the manufacturability and stability needed to serve as a logistically effective solution for deployed personnel and homeland security stockpiling in the event of a bioterrorist act. The ability to both protect against BoNT/A exposure and treat post-exposure disease, combined with the practical aspects that will enable distribution and storage differentiates the product from vaccines and antibodies.

The Economic and Quality of Life Impact of Remote Technologies on High Risk Patients and Their Caregivers

The St. Francis Healthcare Foundation has received funding for a research project that will compare clinical outcomes, economic impacts, and quality of life in a population of end-stage renal disease patients undergoing dialysis. The randomized clini-

cal trial compares the use of remote technologies (RT) and a personlized plan of care to a usual care scenario. The RT intervention includes commercial off-the-shelf home monitoring equipment that is HIPAA compliant, broadband enabled, and capable of interactive video teleconferencing. The device captures and stores patients' weight, blood pressure, and pulse rate. By determining RT efficacy, this research has the potential to improve health outcomes and reduce healthcare expenditures for the DoD and VA.

This device will utilize off-the-shelf technology and Archinoetics-developed hardware to produce an integrated, unobtrusive monitoring/ communication capability.

Broadband Respiratory Virus Surveillance

TATRC funding has established a Respiratory Virus Surveillance Laboratory at TAMC. In partnership with Science Applications International Corporation (SAIC), TAMC is home to the Ibis T5000, a unique system for identifying viruses, bacteria and other organisms. This same system was used in April 2009 to identify Swine Flu in San Diego County, and will be fundamental in establishing preventive medicine strategies and viral surveillance throughout the Pacific Rim.

TAMC is collaborating with SAIC and Ibis Biosciences to develop rapid and specific assays for identification of respiratory viral pathogens. Near real-time assays derived from patients with respiratory illness will be developed to rapidly and specifically identify viral strains as they emerge.

Portable Hazardous Agent Detection (PHAD)

TATRC funding has brought Self Actuating Signal Producing (SASP) technology to Hawaii through Black Ivory Biotech Inc. This new technology aims to improve the selectivity, sensitivity, and threshold of detection for Anthrax outside the laboratory. Given the military's current dependence on stationary detection devices, successful proof of concept here would promote development for this and other portable assays to help in the detection of chemical, biological and other agents with a focus on public health risks.

HFHCN Representative Publications

Ooi EE, Gubler DJ. 2009. Dengue in Southeast Asia: epidemiological characteristics and strategic challenges in disease prevention. *Cad Saude Publica*. 25 Suppl 1: S115-24.

McLaughlin CR, Tsai RJF, Latorre MA, Griffith M. Bioengineered corneas for transplantation and in vitro toxicology. *Frontiers in Bioscience*. 2009; 14: 3326-3337.

Fagerholm P, Lagali NS, Carlsson DJ, Merrett K, Griffith M. Corneal regeneration following implantation of a biomimetic tissue-engineered substitute. *Clin Transl Sci*. 2009; 2: 162–4.

Liu W, Deng C, McLaughlin CR, Fagerholm P, Lagali NS, Heyne B, Scaiano JC, Watsky MA, Kato Y, Munger R, Shinozaki N, Li F, Griffith M. Collagen-phosphorylcholine interpenetrating network hydrogels as corneal substitutes. *Biomaterials*. 2009; 30: 1551-1559.

Nishimura, E. M., Russell, C. A., Stautzenberger, J. P., Ku, H., and Downs, J. H. In-Helmet Oxy-hemoglobin Change Detection Using Near-Infrared Sensing. In: Foundations of Augmented Cognition. *Neuroergonomics and Operational Neuroscience*. Springer-Verlag, Berlin, 2009; 504-513.

Neurotoxin Exposure Treatment Parkinson's Research Program (NETPR)

A Model of Neuronal Venerability and Resilience

The Neurotoxin Exposure Treatment Parkinson's Research Program (NETPR) portfolio was initially established through congressional special interest funding in the 1997 fiscal year appropriation. The program is managed as a dual-use program. The portfolio advances understanding of Parkinson's Disease (PD) progression and develops means of diagnosis, prevention, and therapeutic intervention for both dopamine and non-dopamine responsive symptoms, thereby enhancing strategies for treatment of motor and non-motor conditions that affect quality of life and performance for PD patients. For military service members, the research outcomes are leveraged to support long-term health and performance benefit through an increased understanding of biologic mechanisms underlying potentially harmful military exposures, development of information on the safety of chemicals and drugs used in military operations, means of measuring environmental impacts on performance, development of methodological investigative techniques, enhancement of interdisciplinary collaboration, and improvements in materiel design to reduce potential risks of military exposures.

Key tenets supporting portfolio advance are that alterations in any neurotransmitter system must impose compensatory alterations in other physiologic systems and that the motor aspects—the prime clinical diagnostic criteria of PD—are the result of convergent alterations, which are themselves the result of varied initiating vulnerabilities within the affected population. The inherent limitations of individual genetic inheritance, with an array of combinatorial effects consistent with requirements for biologic differentiation, provides diverse opportunities for environmental modulation and presentation of diverse dysfunctional clinical manifestations in a heterogeneous population.

The program's focus (determination of neurodegenerative mechanisms and related compensatory effects that compromise motor, autonomic and cognitive systems) clarifies why damage to these systems, which are characteristic of the disease in Parkinson's patients, also provides information relevant for potential performance and health risks for military personnel from similar military exposures. Some useful examples, in this abbreviated review of the portfolio's dual-use outcomes, include:

- Development of compounds, acting on intercellular signaling, for treatment of organophosphate exposure. Organophosphate insecticides and pesticides are a suggested risk factor for development of PD as well as a basis for models of the disease. In the military, insecticides and pesticide use is widespread as a means of countering vector borne diseases; and effects on acetylcholine esterase is the primary mode of action of nerve agents.

"The only reason we are involved in these research programs is to make sure we are doing everything we can to take care of the kids coming back from future deployments."

Stephen Grate, D.V.M
Program Manager

NETPR FAST FACTS FY97 - FY09

$279,750,000
187 Funded Projects
1,200 Credited Peer-Reviewed Publications

This program initiated federal and private focus on PD research. Multiple benefits to PD research & DoD for TBI, neuroprotection, neuropsychiatric, and monitoring initiatives

NETPR Significant Accomplishments

- Investigated specific links between environmental exposure and risk factors for Parkinson's disease.
- Identified residual organochlorine compounds in human brain tissue that correlate with development of PD signs.
- Determined molecular mechanisms in dopamine regulatory systems that influence development of dyskinesia.
- Improved methods of neuroimaging for diagnosis and therapy.
- Identified potential variants in genetic markers that affect disease progression in PD models.
- Optimized tests to define non-motor cognitive outcomes that will help in developing rehabiliative treatments for civilian and military patients.
- Developed research strategies to improve quality of life and performance of Parkinson's patients, including dietary, exercise, and lifestyle factors to slow disease progression.
- Developed interdisciplinary studies to separate environmental and genetic impacts on disease progression.
- Funded initial studies to identify peripheral markers of disease.
- Leveraged findings from Parkinson's research to support health and performance of military personnel.

- Development of compounds to treat co-morbid conditions frequent in Parkinson's patients (depression, anxiety disorders, executive function disorders, and sleep dysfunction). Depression and anxiety disorders can be a significant complication in militarily relevant conditions such as PTSD and executive dysfunction was a problem for many Veterans following the '91 Persian Gulf deployment. Irregularities in sleep are also a potential problem for military service personnel due to extreme operational tempo of many deployments.
- Optimization of available means for monitoring central nervous system function, primarily anecdotal clinical correlations with epidemiological findings, neuropsychological assessments to aid in determination of specific domain dysfunctions, various types of molecular and anatomical imaging, and other biomolecular markers and reporters of specific central nervous system and autonomic nervous system function. Neuropsychological domain functions are particularly relevant in both neurodegenerative conditions and for individuals suffering psychological or physiological alterations of brain function. The ANAM instrument, initiated through a joint military service program, is currently demonstrating alterations in neuropsychological measures, during progression of PD, that correlate with alteration in dopamine transporter single photon emission computed tomography (SPECT) imaging. A subset of the ANAM library was optimized to provide baseline and post-injury neuropsychological measures of service personnel, which are imperative in development of relevant rehabilitative efforts on Service Members that suffer traumatic head injuries. All Warfighters are now receiving base-line neuropsychological assessment of domain functions relevant to determining post-deployment performance.
- Determination of specific alterations associated with exercise that are correlated with slowing

progression of Parkinson's and which may be exploited to enhance resilience of service personnel against the stress and hazards of deployment.

- Recent exciting projects in the portfolio involve interdisciplinary studies that promise an ability to separate environmental and genetic aspects affecting progression of the disease, development of pre-clinical diagnostic methods (prior to motor alterations) and a means of identifying peripheral compartment reporter molecules indicative of anatomical and, in some areas, cell-specific central nervous system alteration. This research, in addition to providing the promise of diagnostic and prognostic surrogate markers, based on variations in disease progression and patient vulnerability subset, has the potential to identify specific areas of brain injury in service personnel suffering deployment related injuries.

As the risk factors for PD, noted in epidemiological research, include many of the hazards in operational environments (e.g., organophosphates, organochlorine compounds, head trauma, certain solvents, etc.), research in the portfolio provides a basis for developing spin-offs that enhance the safety and well being of military service members. The improved understanding of the pathophysiology of neurodegenerative changes permits a basis for identifying associated risks of military hazards and development of preventive strategies and treatments which, in turn, suggest additional areas for research that can be exploited to clarify the natural progression of Parkinson's Disease.

NETPR Representative Publications

Bronstein J, Carvey P, Chen H, Cory-Slechta D, DiMonte D, Duda J, English P, Goldman S, Grate S, Hansen J, Hoppin J, Jewell S, Kamel F, Koroshetz W, Langston JW, Logroscino G, Nelson L, Ravina B, Rocca W, Ross GW, Schettler T, Schwarzschild M, Scott B, Seegal R, Singleton A, Steenland K, Tanner CM, Van Den Eeden S, Weisskopf M. Meeting report: consensus statement-Parkinson's disease and the environment: collaborative on health and the environment and Parkinson's Action Network (CHE PAN) conference 26-28 June 2007. *Environ Health Perspect.* 2009; 117: 117-21.

Flajolet, M, Wang, ZL, Futter M, Shen W, Nuangchamnong N, Bender J, Wallach I, Nairn AC, Surmeier DJ, Greengard P. Direct interaction of a G-Protein-Coupled receptor with a receptor tyrosine kinase results in synergistic ERK-mediated biological responses. *Nature Neurosci.* 2009; 11: 1402-1409.

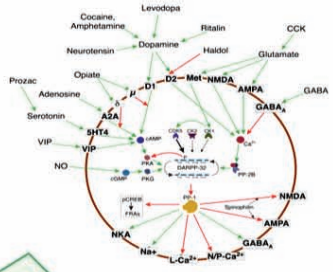
Marek K, Jennings D, Tamagnan G, Seibyl J. Biomarkers for Parkinson's disease: tools to assess Parkinson's disease onset and progression. *Ann Neurol.* 2008; 64 (Suppl 2): S111-21.

Warner-Schmidt JL, Flajolet M, Maller A, Chen EY, Qi H, Svenningsson P, Greengard P. Role of p11 in Cellular and Behavioral Effects of 5-HT4 Receptor Stimulation. *J Neurosci.* 2009; 29: 1937-1946.

Yang L, Zhao K, Calingasan NY, Luo G, Szeto HH, Beal F. Mitochondria targeted peptides protect against 1-methyl-4-phenyl-1,2,3,6-tetrahdropyridine neurotoxicity. *Antioxid Redox Signal.* 2009; 11: 2095-104.

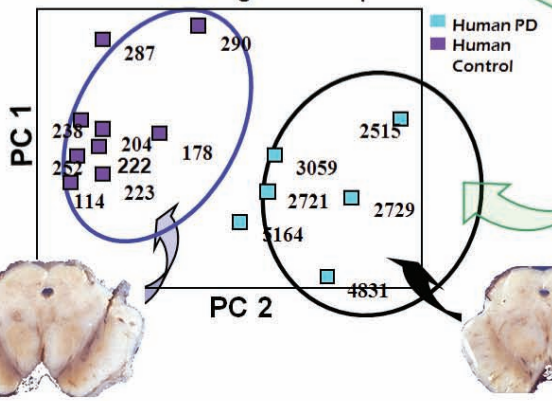
Yu L, Shen HY, Coelho JE, Araújo IM, Huang QY, Day YJ, Rebola N, Canas PM, Rapp EK, Ferrara J, Taylor D, Müller CE, Linden J, Cunha RA, Chen JF. Adenosine A2A receptor antagonists exert motor and neuroprotective effects by distinct cellular mechanisms. *Ann Neurol.* 2008; 63: 338-46.

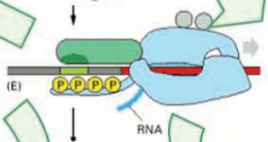
Identification of Vulnerability Subsets



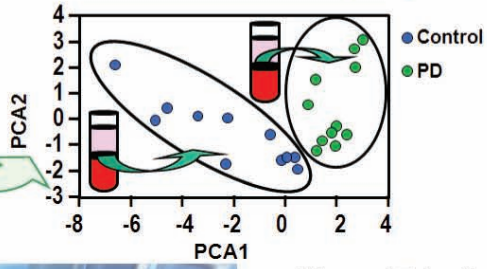
Signaling pathways (in the neostriatum)1

Principal Components Analysis of Control vs. PD Substantia Nigra Transcripts2





Principal Components Analysis of Control vs. PD WBC Transcripts 3, 4



Mhyre and Federoff, unpublished

1 Courtesy of Dr. Paul Greengard, Rockefeller University and Dr. Allen Fienberg, ITI, Inc.

2 Miller RM, et al., Neurobiol Dis. 2006 Feb;21(2):305-13.

2, 3 Figures developed by Dr. Howard Federoff, Modified for presentation

4 Mhyre and Federoff, unpublished

5 Figure from: Alberts, Johnson, Lewis, Raff, Roberts, & Walter, *Molecular Biology of the Cell, 4th Edition*, Garland Science, New York, NY (2002).

This diagram highlights the primary focus of NETPR. Correlation of genetic and environmental impacts on cellular function allows identification of biomarkers, vulnerable populations, and cellular targets for therapeutic interventions.

Northern California Institute for Research and Education (NCIRE)

www.ncire.org

A Collaborative Center for VA-DoD Research on Brain and Behavioral Health

The Neuroscience Center of Excellence (NCE) is a unique research partnership between TATRC and the Northern California Institute for Research and Education (NCIRE). NCIRE - The Veterans Health Research Institute is a collaborative institute that supports and facilitates biomedical research, basic through translational, at the SFVAMC and the University of California-San Francisco (UCSF) on behalf of America's Veterans and active duty military personnel. The NCE provides additional research capacity, complementing DoD resources through efforts that include state-of-the-art high-field neuroimaging at the Center for Imaging of Neurodegenerative Diseases (CIND), located at SFVAMC. Over 200 researchers and approximately 425 affiliates and administrative/support staff make up NCIRE.

The NCE was established to bring VA, DoD, university, and industry resources together to build on NCIRE's core research strengths in neuroimaging, neurorehabilitation, PTSD, TBI, sleep and human performance, and telemedicine. Its aim is to bring experts in individual specialties into focused alliances in order to hasten the development of the health services most crucial to the health and well being of Warriors.

NCIRE's research program benefits from a comprehensive view of the entire life course of military personnel, from preparation and training, predeployment, and management of mental and physical stressors in the combat theater, to recognition and treatment of post-deployment health concerns. The NCE has become an exemplar of seamless interagency cooperation and collaboration, and a model for effective partnerships.

To date, TATRC funds have supported more than 40 research projects at NCIRE. In addition, a number of related projects leverage TATRC-supported personnel and research infrastructure to bring added value to NCIRE's overall research effort.

Identifying Brain Biomarkers for PTSD

A number of neurological and psychiatric conditions have been demonstrated to be associated with structural and/or functional changes in the brain. Recent progress in delineating the underlying substrates for these conditions has been made using magnetic resonance imaging techniques. In a recent series of TATRC funded studies, Dr. Norbert Schuff compared hippocampal brain regions in Veterans suffering from chronic PTSD with age-matched controls. The results of this study demonstrated that in Veterans with PTSD, there was significant atrophy of the CA3/dentate gyrus subfields in the hippocampus—areas associated with stress and memory dysfunction. The hippocampus is one of the few brain regions with significant neurogenesis potential, which offers a potential therapeutic approach to preventing or reversing brain atrophy. This finding is an important step on the road to establishing robust brain biomarkers for PTSD.

NCIRE FAST FACTS FY03 - FY09

- 31 active projects
- 11 completed projects
- 37 PIs involved in these projects
- 37 publications to date
- $5 million FY 2009 budget

Establishing a Program to Swiftly get OIF/OEF Veterans into Mental Health Treatment without Stigma

Accessing medical services is critical in the recovery process for any injury. A recent TATRC-funded study ("Vets Return Home") by Dr. Karen Seal used telephone-based assessments to screen OIF/OEF Veterans for mental health symptoms and uncover their barriers to receiving care at both VA and community agencies. Results suggest that using Motivational Interviewing techniques to explore their ambivalence about seeking treatment has lead a significant number of Veterans to contact and attend mental health services provided by the VA and other community-based agencies. This study has been expanded by the VA and is currently in the process of partnering with other veteran service organizations to broaden treatment focus. The success of this approach demonstrates the value of tele-psychiatric approaches and telemedicine in bringing health services to populations that are difficult to reach.

Identifying Potential Molecular Targets to Protect Brain from Post-TBI Inflammation

Brain and spinal cord injury are devastating injuries in both military and civilian personnel. The damage to the nervous system caused by traumatic events result from both the initial physical injury and the delayed biochemical processes that follow. Inflammation following brain injury is thought to result in significant secondary loss of neurons and prevents formation of new neurons, exacerbating post-TBI brain damage. In an experimental model of stroke, Dr. Raymond Swanson confirmed that inhibition of the enzyme PARP-1 suppresses inflammation, reduces neuron death, and promotes neurogenesis in the hippocampus. As a consequence of this protection of existing brain cells and the development of new neurons, there was a significant functional improvement in memory. Studies are currently under way using this research approach to discover effective therapies for TBI and spinal cord injuries.

Clockwise from above: Mr. Bob Obana, NCIRE Executive Director, introduces a VTC presentation from Iraq by LTC Sloane Guy at the NCIRE Investigators Day presentations on the "Brain at War."

BG Loree Sutton (center), Director of the DCoE, in an after action summary at NCIRE.

Dr. John Carney, the TATRC COR for the NCIRE projects, discusses drug development efforts with LTC Jay Stone from DCoE.

Identifying Markers of Predisposition/ Resilience to PTSD in Police Officers and Other First Responders

In multiple studies with police, emergency personnel, and other first responders, Dr. Charles Marmar has begun to build a detailed picture of PTSD susceptibility and resiliency. Peritraumatic dissociation, peritraumatic emotional distress, greater use of escape-avoidance, and self-control coping are associated with higher post-traumatic stress symptoms. In contrast, fewer years of experience, poorer overall adjustment, greater external locus of control, and poorer social support are associated with greater levels of stress-specific and general psychiatric symptoms. Shorter length of service is also associated with greater peritraumatic emotional distress. Female emergency services personnel report lower critical incident stressor exposure, but higher levels of general distress. Conversely, resilience is associated with factors such as adaptive personality traits, coping strategies, and a sense of personal control over one's fate. Emergency services workers who have a strong internal sense of identity, well defined goals for the future, high ambition, and who use active problem solving rather than avoidant coping strategies are less emotionally disturbed at the time of a traumatic exposure and in the months and years beyond. This work suggests possible targets for pre-trauma training and/or post-trauma treatment for military personnel.

NCIRE Representative Publications

Hsu JY, Bourguignon LY, Adams CM, Peyrollier K, Zhang H, Fandel T, Cun CL, Werb Z, Noble-Haeusslein LJ. Matrix metalloproteinase-9 facilitates glial scar formation in the injured spinal cord. *J Neurosci.* 2008; 28: 13467-77.

Seal KH, Metzler TJ, Gima KS, Bertenthal D, Maguen S, Marmar CR. Trends and risk factors for mental health diagnoses among Iraq and Afghanistan Veterans using Department of Veterans Affairs health care, 2002-2008. *Am J Public Health.* 2009; 99: 1651-8. [Epub 2009 Jul 16.]

T. Kauppinen, et al. Inhibition of poly(ADP-ribose) polymerase suppresses inflammation and promotes recovery after ischemic injury. *Journal of Cerebral Blood Flow and Metabolism.* 2009; 29: 820–928.

B.E. Cohen, et al. Post-traumatic stress disorder and health-related quality of life in patients with heart disease: Findings from the Heart and Soul Study. *Arch Gen Psychiatry.* 2009; 29: 820-829.

N. Schuff. The value of high field MRI for studies of Parkinson's disease. *Journal of Movement Disorders.* 2009; 24: S684-S690.

"We must never forget the reason that we explore the most cutting-edge equipment, methods, and treatments... our military men and women, and especially our wounded Warriors deserve the best. We are honored to be in the service of these great heroes. If through the technologies and scientific advancements facilitated by TATRC we can make their lives better, then our mission has been successful."

Brenda Bart-Knauer, M.D.
TATRC Program Manager

Samueli Institute

www.siib.org

Warrior Wellness Models that put Warfighters in Charge of Their Own Health

Since 2003, the Samueli Institute has teamed with DoD to develop a model of integrative health, and conduct research and program evaluations on the efficacy of complementary and alternative medicine (CAM). Altogether, the goal of the Institute is to transform health care through the scientific exploration of healing, where healing becomes the formative concept for achieving and maintaining wellness and ameliorating chronic disease. Concepts of healing, healing environments, flourishing in the midst of disease, maintaining wellness, reintegration into society, and wholeness have been extensively explored through Samueli projects, including many for the military.

The military projects are divided into five main multi-year programs; however, there are many key accomplishments to report for 2009 to include, several peer-reviewed publications and presentations, nationally and internationally.

Partnering With Experts

Over the past 20 years there has been a surge in the use of CAM in developed countries. DoD personnel are seeking alternative methods of therapeutic interventions, such as prevention, wellness, exercise, healthy diet, and self empowerment. This is evidenced by the increasing number of Veterans who, diagnosed with physical or mental injuries, are pursuing alternative treatment approaches.

The Institute is one of the largest non-profit organizations solely devoted to investigating core questions about healing. It has developed public and private partnerships with organizations, and research institutions nationally and internationally. It is the primary organization for conducting research on CAM for the DoD and VHA.

Defining Research Directions

Under the aegis of the five military research programs, with major scientific input and managerial oversight from TATRC, the Samueli Institute is conducting research and program evaluations on the efficacy of CAM. To streamline this process the Institute has developed an integrating concept, the Warrior Wellness Integrated Information Network (WIN2), which describes the framework for military medical research.

It is an organizing framework which provides a central, systematic and efficient process for screening, selecting, monitoring and directing total fitness practices across Service Members' military life cycle. The Institute uses components of the WIN2 throughout the five military-funded programs to provide the DoD with a systematic criteria-based process for screening and selecting new total performance fitness programs and practices, evaluating current programs, monitoring outcomes and impact, and translating and disseminating information to a human performance optimization clearinghouse for use by Service Members, commanders, medical personnel, and DoD leadership, so they determine their mission appropriateness.

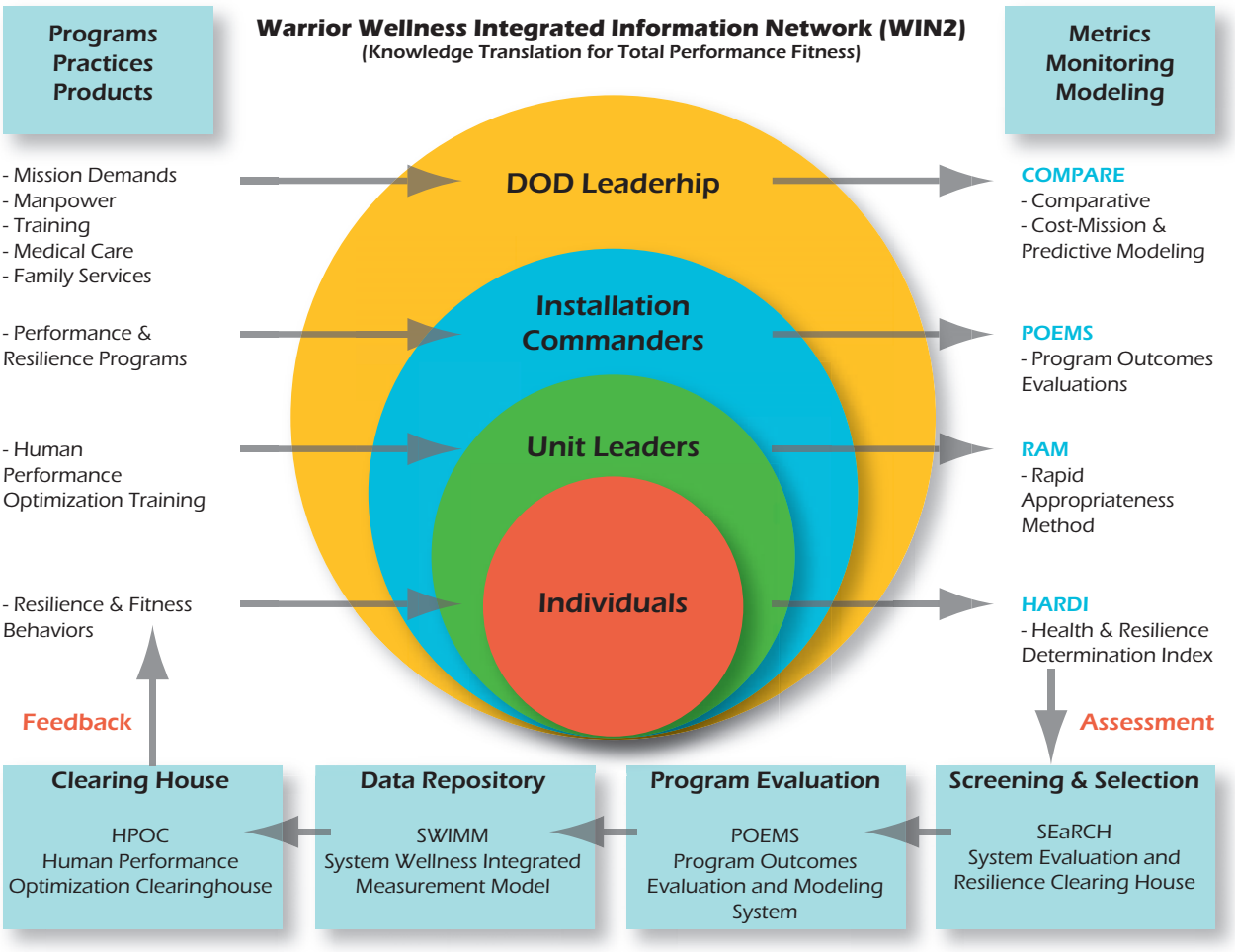
SAMUELI INSTITUTE
EXPLORING THE SCIENCE OF HEALING

MIL-VET

The objectives of the MIL-VET Program are to implement and administer a series of specific research projects evaluating the feasibility, safety, effectiveness, efficacy, mechanisms, policy issues, and cost-benefit of integrative medicine. The MIL-VET Program investigates the value of selected CAM therapies for the prevention and treatment of conditions that have direct and immediate military and civilian relevance and application, such as musculoskeletal pain, acute pain, stress, chemical and biological toxin exposures, brain and tissue injury, and selected chronic conditions in both military and civilian populations. By conducting the majority of its projects through partnership with military treatment facilities and laboratories, in field training and combat environments, and by including civilian CAM experts, conventional clinicians and experienced researchers in its programs, MIL-VET will optimize the discovery and knowledge transfer of CAM and integrative medicine research and maximize the benefits of this research for military and civilian populations. To date, the MIL-VET research activities include systematic reviews; retrospective and prospective outcomes studies; randomized, controlled clinical trials; research conferences; program evaluations; basic science/laboratory studies (*in vitro* and/or animal); and surveys.

Metabolic Defense (MET DEF)

The aims of the MET DEF program are to conduct research on dietary supplements in military operations and healthcare to establish and administer the premier national research program on the safety, efficacy and mechanisms of dietary and nutritional supplement (DNS) practices of potential importance



The purpose of the WIN2 is to collect and translate knowledge on the factors that contribute to total performance such as, health, resilience, and human performance enhancement, for Service Members.

"The time has come to create a new model of health care delivery that makes room for both healing and cure."

Wayne Jonas, M.D.
Samueli Institute

to military operations and populations. The long-term goal of this initiative is to establish a dynamic database of DNS categories of special interest to the military, develop guidance for the rigorous and efficient evaluation of the clinical efficacy of DNS, and develop a strategy for the exploration of DNS combinations to address identified needs. The work is conducted in collaboration with military partners, ensuring that project results will have direct and immediate military relevance and application. The program will produce a comprehensive analysis of DNS issues that are important to the military, assess the state of the science relating to performance-enhancing, anti-inflammatory, anti-infection and immunoactive DNS, and will develop a strategy for assessing the effects of selected multiple-ingredient supplement formulas that may provide broad benefit to military personnel in combat and field environments.

Integrative Medicine, Communication, Compassion and Chronic Care Program (IC4)

The long-term goal of the IC4 Program is to improve chronic disease care by enhancing the provider team-patient encounter and interaction. The objectives are to conduct research to produce:

- increased understanding and skills in communication;
- more coherence and cohesion in the patient care team and the medical encounter;
- improved satisfaction of all parties in chronic disease management;
- improved delivery of integrative medicine;
- better intermediate and long term clinical outcomes compared with controls; and
- reduced costs compared to current health care delivery.

The IC4 Program will develop and test an innovative, coordinated approach to the delivery of com-

munication, compassion and integrative medicine in education and practice settings in both military and civilian sectors.

Center for Research on Integrative Medicine (CRIMM)

The objective of the Center for Research on Integrative Medicine (CRIMM) is to identify an integrative biopsychosocial program for the management of stress focused on skills training of combat troops and their families in four key areas: physical, social, mental, and spiritual. The specific aims of CRIMM are to:

- gather best evidence on the most reputable and scientifically advanced programs of biopsychosocial preset and reset training, and rigorously assess the most promising ones for use in a military populations;
- synthesize the evidence for the best programs, and make a recommendation for program configuration and implementation;
- assess the needs of combat-exposed military personnel and their families at key military training sites and readiness of these environments to participate in such programs;
- develop a valid and reliable toolkit for assessing such programs;
- launch a pilot program incorporating the biopsychosocial model within an appropriate training and education environment; and
- evaluate the cost, timing, and outcomes of the training to provide military decision makers with the evidence to determine whether expansion of such training will effectively support the mind-body-spirit of our nation's Warriors.

In addition to programs supported through TATRC, CRIMM has other related DoD efforts such as an evaluation of the Warrior Optimization System (WAROPS) resilience program at Fort Carson and the Auricular Stimulating Procedure (ear acupuncture) training program in the Air Force.

MIL-CAM

The MIL-CAM research program systematically focuses research and communication on CAM in the military to provide the DoD, VHA, and the public with evidence needed to determine the safety, effectiveness, mechanisms, and appropriateness of CAM practices for these populations and public health in three main areas of critical importance for military personnel and our healthcare systems: performance enhancement, management of stress and related disorders, and pain and chronic disease management.

Samueli Institute Representative Publications

Arun P, Ariyannur PS, Moffett JR, et al. Metabolic acetate therapy for the treatment of traumatic brain injury. *J Neurotrauma.* 2010; 27(1): 293-8.

Crawford CC, Huynh MT, Kepple A, Jonas WB. Systematic assessment of the quality of research studies of conventional and alternative treatment(s) of primary headache. *Pain Physician.* Mar-Apr 2009; 12(2): 461-470.

Giordano J. Pain, depression, brain-mind, and healing: the potential complementarity of process and purpose. *The Pain Practitioner.* 2008; 18(2): 7-12.

Niemtzow R, Burns S, Cooper J, et al. Acupuncture clinical pain trial in a military medical center: outcomes. *Medical Acupuncture.* 2008; 20(4): 255-261.

Ananth S. CAM: An increasing presence in US hospitals. Hospitals & Health Networks. 2009; http://www.hhnmag.com/hhnmag_app/jsp/articledisplay.jsp?dcrpath=HHNMAG/Article/data/01JAN2009/090120HHN_Online_Ananth&domain=HHNMAG.

Samueli Institute Representative Accomplishments by Program Areas

MIL-VET

• Developed the SEaRCH (Scientific Evaluation and Review of Claims in Healing) strategy to systematically and rigorously evaluate CAM practices, therapies and claims to determine if they warrant further investigation.

• Developed a survey tool and process which was used to complete a pilot study of hospital healing environments to understand the nature and prevalence of programs currently in use.

• Conducted an analysis of patient-based assessment (PBOA) instruments in acupuncture research and discovered the five most common instruments used in over 250 reports.

• Evaluated outcomes in a VA Integrative Health Clinic for nonmalignant pain treatment.

MET-DEF

• Conducted a DoD-wide survey of dietary supplement use in collaboration with US Army Research Institute of Environmental Medicine (USARIEM).

• Organized and conducted a successful webcast national symposium on omega-3 fatty acids collaboratively with DoD, NIAAA, and DARPA entitled "Nutritional Armor for the Warfighter: Can Omega-3 Fatty Acids Enhance Stress Resilience, Wellness, and Military Performance?"

IC4

• Completed a systematic review on program evaluations on healing relationships in hospital settings.

• Completed a study on the current state of research on physician communication.

• Conducted an analysis on the information gaps in peer-reviewed literature on the effects of provider/patient relationship on healing, and education and training programs to improve patient-provider and provider-provider relationships in health care settings.

CRIMM

• Developed a rigorous military clinical CAM program evaluation methodology.

• Developed a specific protocol for program evaluation and a draft of an evaluation toolkit that will be adaptable to evaluations in a variety of settings.

• Conducted site visits to military posts to meet with military leaders and medical providers to provide information and conduct needs assessment on integrative, biopsychosocial programs for stress and reintegration management.

MIL-CAM

• Co-organized the 5th Annual Whole Systems Research (Island) Group Meeting, "Creating Collaborative Relationships: Whole CAM Systems and Complexity Research," to develop a framework for an integrated model for the evaluation of healing.

• Presented on findings in optimal healing Environments at the Military Health Research Forum and at the 12th Annual Force Health Protection (FHP) Conference.

Vision Research Program

www.visioncenterofexcellence.org

Support to the Interagency DoD/VA Vision Center of Excellence

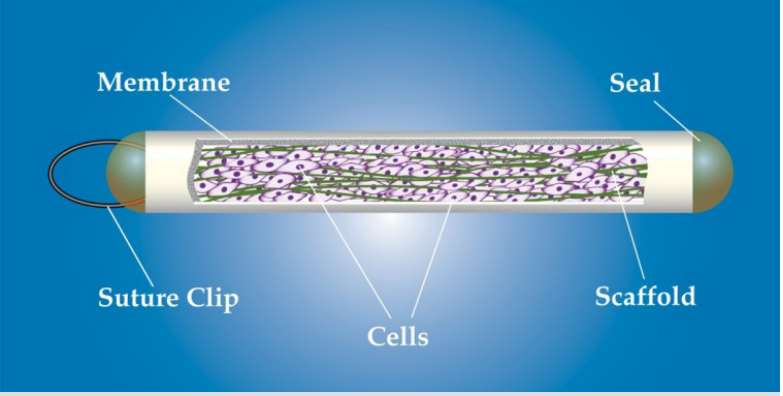
The longstanding TATRC portfolio encompassing vision and eye trauma projects found a new key customer and significant transition point in 2009 with the congressionally-mandated Defense Center of Excellence for Vision. The portfolio has targeted eye damage and diseases that result in degeneration of the critical components of the eye and loss of vision. This includes progressive problems associated with diabetes and other diseases, as well as acute and later phase damage associated with combat head injuries. This year, congressional funding was provided for a competitive research program that focused on eye damage associated with brain injury following blast exposure. Additional funds were provided by the Clinical and Rehabilitation Medicine research program (RAD4), and projects were solicited on behalf of the DCoE-Vision, RAD4 and the Combat Casualty Care research program (RAD2), and with the assistance of the service leaders in ophthalmology and optometry. The aim of the Vision portfolio is to assess new technologies and therapies that address the ocular issues of our Service Members.

COL Donald Gagliano, Ophthalmologist and Executive Director of the VCE, examines the eyes of a patient using a slit lamp. The slit lamp is a microscope with a light attached that allows the doctor to view the anterior structures of the eye such as the cornea, iris, and lens. With special lenses, it is possible to examine the vitreous and the back of the eye as well.

The Vision Center of Excellence (VCE) and an accompanying Military Eye Injury Registry were provisions of the Military Eye Trauma Treatment Act (METTA) that were included in Fiscal Year (FY) 2008 National Defense Authorization Act, passed in late January 2008. The VCE addresses prevention, diagnosis, mitigation, treatment, and rehabilitation of military eye injuries, and will coordinate work on the Defense and Veterans Eye Injury Registry (DVEIR). The Center also facilitates vision research, including research on prevention, visual dysfunction related to TBI, and military eye injuries. The DVEIR will track the occurrence, treatment and outcomes of all eye injuries or visual dysfunction experienced by service members who have served on active duty since September 11, 2001. The DVEIR will be the first major registry linking the DoD's health information system, AHLTA, with the VA's health information system, vistA, the Veterans Health Information System and Technology Architecture. Data collected in the DVEIR will allow the VCE to develop initiatives to focus research more effectively, evaluate DoD/VA health care processes, and establish guidelines for care, among other improvements. As the VCE evolves, the DVEIR and other initiatives are expected to increase awareness of eye injuries and visual dysfunction throughout the services and Veterans' organizations, foster promising research and provide a more seamless transition of care within and between DoD and VA.

VISION RESEARCH FAST FACTS FY00 - FY09

- 12 Projects
- 28 Publications
- 25 PI's
- 26 Invited Presentations



Neurotech's Encapsulated Cell Technology (ECT) uniquely enables the controlled, continuous delivery of biologics directly to the back of the eye, overcoming a major obstacle in the treatment of retinal disease.

National Eye Evaluation Research (NEER) Network for Clinical Trials in Retinal Degenerative Diseases by the National Neurovision Research Institute

Stephen Rose, PhD, is leading the NEER effort in establishing a network of five clinical treatment and evaluation centers (CTECs) to study retinal degenerative diseases. Retinal degenerative diseases are a family of inherited pathologies with the ultimate consequence of photoreceptor apoptosis and severe visual impairment usually ending in blindness. The network advances the science of therapeutic and preventive interventions for inherited orphan retinal degenerative diseases and dry age related macular degeneration through the conduct of clinical trials. The fives centers are: the University of Medicine and Dentistry of New Jersey, the Children's Hospital of Philadelphia, the Wilmer Eye Institute at Johns Hopkins University, the University of California at San Diego, and the University of Utah Moran Eye Center.

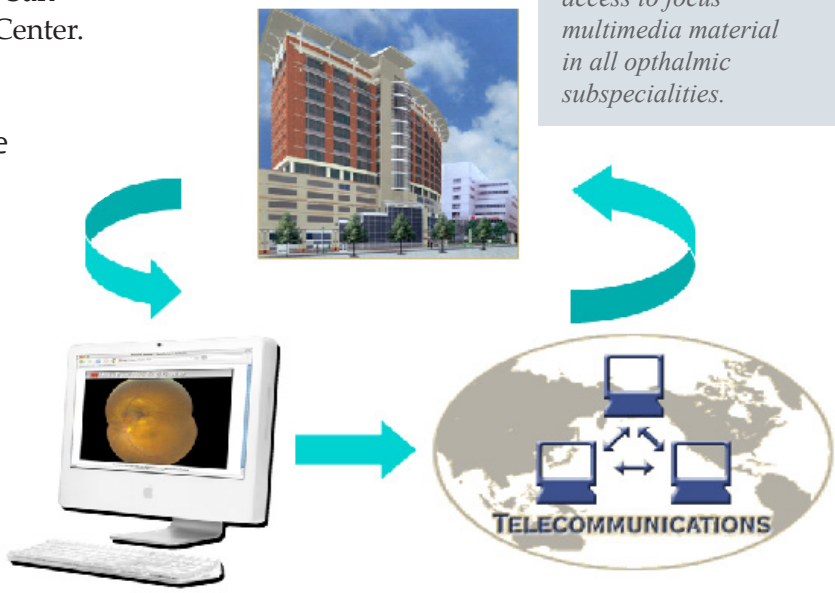
Tele-ophthalmology: Enhancing Care and Education for Military Medicine at Wills Eye Institute

Robert Sergott, MD, and his researchers are establishing a cost-effective platform that will rapidly diagnose patients with common, costly diseases such as diabetes mellitus and other complicated ophthalmologic problems. The same technology will be used for the online education resource and the ophthalmology imaging academy - distance learning programs.

Patients attending the medical and endocrinology clinics at Madigan and Landstuhl Army Medical Centers, the health clinics at Grafenwoehr and Brussels and patients at Jefferson University Health System in Philadelphia will be screened with non-mydriatic, 45-degree fundus photography.

- **Online Educational Resource:** The Educational Portal is available to all medical military personnel. Email notifications are sent to all members of the Society of Military Ophthalmology as new materials are posted each month. The site has been redesigned to feature videos of surgical procedures in addition to lectures and other presentations.
- **Ophthalmology Imaging Academy:** Construction for the space at Wills Eye Institute to house the new imaging center was completed, the equipment was installed and the facility opened in May 2009. The first course was held in September 2009.

The "Wills without Walls" solution promotes continuing medical education during wartime by providing secure, worldwide access to focus multimedia material in all opthalmic subspecialities.



Military Vision Research Program at the Schepens Eye Research Institute (SERI)

Dr. Paul Sternberg gives an injection into the eye of a patient using a new medicine for people over 55 in the Vanderbilt Eye Institute. (Vanderbilt Photo/Neil Brake)

Darlene Dartt, PhD, and her team are developing new ways to save the vision of Warfighters injured on today's battlefield and to push the frontier of vision technologies forward. To keep abreast of the needs of the military, the Institute holds two-day symposia biannually in which practicing military eye specialists discuss the challenges that they encounter in caring for men and women in uniform with Schepens scientists who then design research programs to respond to their needs. The resulting research, on everything from laser damage to the retina and optic nerve regeneration to corneal bandages and enhanced displays, results in clinically targeted products with enormous potential for both military and civilian applications. Working primarily on long-term goals leading to new or improved technologies, this research program seeks out partners who can stimulate innovation and help open up fresh research areas.

Center for Ophthalmic Innovation (ONOVA) at the Bascom Palmer Eye Institute (BPEI)

Byron Lam, MD, and his colleagues at the University of Miami are establishing a center of excellence with four focus areas:

- **Telemedicine:** Technology is an important part of the solution for blinding eye disease. And it's out there in our universities and industries, waiting to be captured and applied to ophthalmology. It is an unfortunate fact that the amazing potential for medical innovation brought about through recent advances in the biosciences, biomedical engineering, and the human genome project are not being fully realized because of the lack of attention to translational research. This center was created to address this unmet need.
- **Ophthalmic Biophysics:** This program brings Biomedical Engineering Technology to the clinical arena. This includes optoelectronics, mechanics, lasers, and polymer chemistry. The program has a long history of innovative research that has advanced the management of ophthalmic disease, starting with the inception of vitrectomy, a surgical technique that revolutionized ophthalmology. Of particular interest to the military is the work of this group on artificial cornea, implants to treat traumatic injury, novel methods of drug delivery, and laser effects on eye tissue.
- **Molecular Ophthalmology:** The program tackles eye health issues in four technology areas: Biomarkers, Molecular Diagnostics, & Therapeutic Targets; Cellular Therapies & Tissue Engineering; Gene Therapy; and Genomics.
- **Inherited Eye Disease:** The Florida Inherited Eye Disease Project is a collaborative effort with Howard Hughes investigator Dr. Edwin Stone and the University of Iowa's Carver Nonprofit Genetic Testing Laboratory. A network of physicians created across Florida is referring patients with inherited eye disease to BPEI. Genetic testing is being performed, and patients are provided with counseling about their disease. Most importantly, the patient diagnostic information is being entered into

a database, providing a unique resource for implementation of clinical trials to bring novel therapeutics to patients, as they emerge from the MCMI and other research centers across the country and the world.

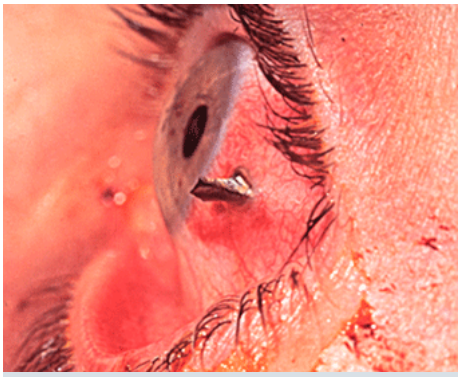
Vision Integrating Strategies in Ophthalmology and Neurochemistry (VISION) at the University of North Texas Health Science Center

Thomas Yorio, PhD, and his unit plan to develop and characterize mouse models of (a) optic nerve crush, (b) retinal ischemia/reperfusion, and (c) chronic pressure elevation to generate defined and quantifiable end points for examining damage to the retina, optic nerve, and visual centers of the brain.

Dr. Yorio and his team will use genomic analysis (microarrays) to identify pathogenic pathways involved in damage to the retina, optic nerve, and visual centers of the brain in all three mouse models of traumatic ocular injury; and initiate neuroprotection studies in the optic nerve crush and retinal ischemia/reperfusion models.

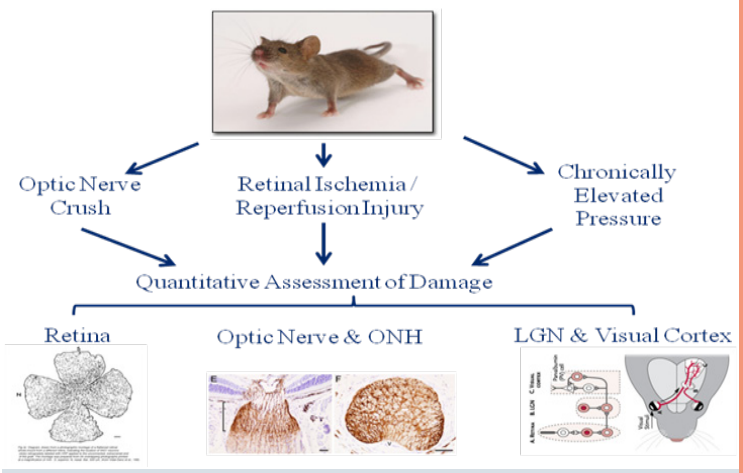
Corneal Wound Healing at St. John's Research Institute

Dr. Shachar Tauber leads this effort to develop solutions for corneal wound repair. Interventions are needed for battlefield injuries to stabilize a cornea following blunt force corneal trauma, missile damage, and/or chemical injury until the patient can be treated at a qualified hospital. Often, ocular damage is deemed secondary to life threatening wounds. Ophthalmologic treatment, at this time, can be delayed by as much as one to three days.



For injuries such as this corneal penetration, an adhesive agent for use in corneal stabilization with sustained drug release properties is being developed.

These aids can readily be administered by a medic to treat the cornea until the patient reaches a hospital where surgery



Phase I of the study is quantifying the damage to the retina, optic nerve and brain vision centers by developing mouse models of (a) optic nerve crush, (b) retinal ischemia/ reperfusion, and (c) chronic pressure elevation.

can be performed. The bandage contact lens can be used in the field by a medic to apply to the cornea to act as a medicated bandage containing therapeutic agents to sterilize the corneal wound, prevent infection and aid in recovery. The mechanical properties of the contact lens will act to mechanically hold the cornea together, as well as preclude the blink reflex from further exacerbating the wound until surgery can be performed. The lens will contain a drug delivery system which can administer therapeutic agents for up to three days.

A wound healing contact lens can also be used to accelerate wound healing by delivering drugs to the eye for a period of 1 week to 3 months based on drug delivery from a contact lens. A number of agents can be administered to solve various physiology issues from the wound.

Bioadhesive glue will be used by the military to treat patients in the field who have disrupted or missing corneal tissue. This glue would hold the cornea together until the patient can reach a hospital and may contain therapeutic agents to stabilize the cornea for repair.

The identification of proteins and levels secreted by the eye during corneal trauma would aid the military in devising therapeutic treatments for corneal injuries which occur in the field. Additionally, this data could be used to accelerate the repair time following PRK to military personnel allowing a faster return to duty.

Peer Reviewed Vision Research Program at TATRC

This year Congress funded eye and vision research as its own distinct research program with a $4M appropriation, and the CCCRP and CRMRP contributed an additional $2M to the effort. The vision committee is chaired by COL Gagliano and includes the military ophthalmology and optometry consultants, directors of TATRC, CRMRP, CCCRP, the VA, FDA, NEI of NIH, the National Alliance for Eye and Vision Research (NAEVR) and the Association for Research in Vision and Ophthalmology (ARVO). Program leaders estimate that six to 10 grants will be awarded in the following critical areas: treatments for TBI associated with visual dysfunction; treatments to slow or stop loss of vision in traumatic optic neuropathies; computational models of mechanisms of primary blast injury to the eye and vision system; methods to test visual dysfunction in the presence of cognitive impairment; and treatments for blast and burn injury to ocular structures.

Illustration of a proposed artifical system featuring UEA implanted in the primary visual cortex.

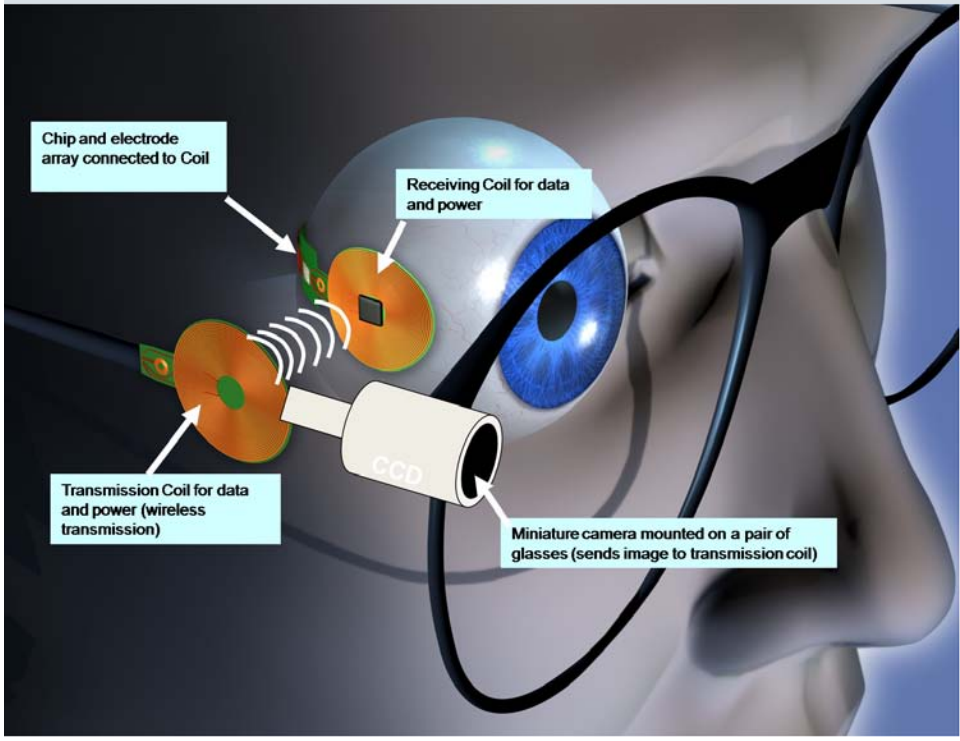
Sight Restoration by Electrical Stimulation of Visual Cortex Via Arrays of Penetrating Microelectrodes at the University of Utah Moran Eye Center

Drs Richard Norman, Brad Gregor, and their colleagues are demonstrating proof of concept whereby the Utah Microelectrode Array will be used to potentially restore limited but useful vision in non-human primates. A systematic experimental approach is being employed to define the design parameters needed to implement a functional visual neural prosthesis, using behavioral responses to indicate what they perceive in response to patterned electrical stimulation of the cortex. Investigators will then determine the design parameters for a functional visual neural prosthesis and study its safety and efficacy.

Novel Retinal Prosthesis at the Massachusetts Eye and Ear Infirmary

Joseph Rizzo, MD, and his group are creating a retinal prosthesis that is designed to restore vision to some blind patients. This device will permit "customizable" adjustments to accommodate the visual needs of each patient and improve their quality of life. The retinal prosthesis will capture visual images, communicate the images to electronic components that interface with the retina, and then selectively deliver electrical pulses to the retina to create vision.

In a sub-retinal prosthesis, the image obtained by an external camera is translated into an electromagnetic signal, then transmitted wirelessly to the implanted secondary data coil attached to the eye.



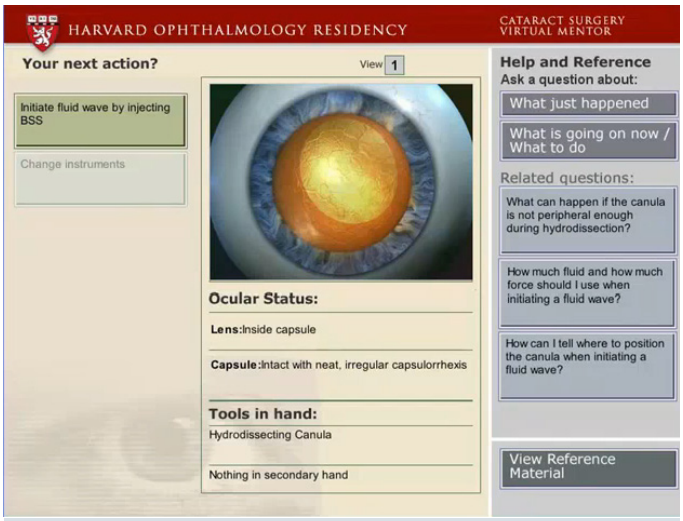
Anthro-Centric Multisensory Interface for Vision Augmentation/Substitution (AMCI-VAS) at the Florida Institute for Human and Machine Cognition

Dr. Anil K. Raj will use the Brain Port® array held against the tongue to indicate high-resolution visual information from in front of the user (i.e., foveal vision). A wider field of view will be presented on the abdomen by the Video Tact™ to provide contextual and registration information relative to the tongue "foveal" information. The Torso Tactile Interface (TTI) will display a low resolution 360 degree representation of the visual environment to enable the user to detect motion and other changes in the visual environment (i.e., peripheral vision) using an array of infrared range sensors worn on the head. Proper use of the ACMI-VAS system will require an orientation session during which the participant is taught how to use the displays. The participants will be able to move their heads to kinematically control the dynamic system (i.e., pan and tilt) to learn to accurately interpret this novel feedback stimuli.

Dr. Raj tests the BrainPort tongue vision system.

Virtual Mentor Cataract Surgery Trainer at the Massachusetts Eye and Ear Infirmary:

John Loewenstein, MD, and his researchers are creating a content-based curriculum to help teach cataract surgery rather than to create another surgical simulator de novo. Computer-based and interactive, the proposed curriculum would pose common conceptual problems to the resident, thereby challenging his critical thinking abilities in a variety of stressful, yet not uncommon surgical situations. The Virtual Mentor would include a library of video links that both demonstrate expert technique as well as discuss various aspects of the simulated scenario more in depth.



This simulation uses 3D animation to support learners as they make sense of their experience. Panels from left to right: select the next action in the procedure, 3D animation and information about the status of the surgery, and access to help and references.

Vision Research Program Representative Publications

Chung ES, Chauhan SK, Jin Y, Nakao S, Hafezi-Moghadam A, van Rooijen N, Zhang Q, Chen L, Dana R. Contribution of macrophages to angiogenesis induced by vascular endothelial growth factor receptor-3-specific ligands. *Am J Pathol.* 2009; 175: 1984-92.

Lei H, Kazlauskas A. Growth factors outside of the PDGF family employ ROS/SFKs to activate PDGF receptor alpha and thereby promote proliferation and survival of cells. *J Biol Chem.* 2009; 284: 6329.

Qiao H, Lucas K, Stein-Streilein J. Retinal laser burn disrupts immune privilege in the eye. *Am J Pathol.* 2009; 174: 414-22.

Chen, J., Shah, H.A., Herbert, C., Loewenstein, J., Rizzo, J.F. Extraction of a Chronically Implanted, Microfabricated, Sub-Retinal Electrode Array. *Ophthalmic Res* 2009; 42: 128-137.

Henderson B, Kim J, Golnik K, Oetting T, Lee A, Volpe N, Aaron M, Uhler T, Arnold A, Dunn J, Prajna NV, Lane AM, Loewenstein J. Evaluation of the Virtual Mentor Cataract Training Program. *Ophthalmology.* 2010; 117(2): 253-8.

Highlighted Projects

TATRC champions projects that have great promise where preliminary data or demonstration of feasibility are lacking. Some potentially important solutions cannot gain support through traditional grant mechanisms because they do not involve an elegant hypothesis, but may involve a "simple" engineering solution for clinical process improvement.

For this year's report, we have chosen a sample of TATRC-supported projects that illustrate this concept of potentially innovative solutions to important military medical problems. This includes two projects dealing with the serious problem of hospital-acquired infections, a problem with renewed importance to the military with imported wound infections. Other projects in this section involve major equipment or database infrastructure development to demonstrate potentially leap ahead technologies in cancer therapy (proton beam therapy, p.142) or acute trauma tissue salvage (hibernation genomics, pp. 132-133). Others organize important programs such as hospital of the future interoperability and patient safety initiatives (pp. 134-141). There is no other agency providing support for the DoD to team with FDA to explore patient safety and cost savings possible with a pharmacoviligance program (pp. 140-141) even though there are no significant technological barriers to making this a practical reality. The entertainment industry has pioneered the use of avatars in immersive systems, yet the medical community has been slow to embrace the familiar technologies of this generation to conduct effective health risk communications such as the use of an online behavioral health resources virtual human "coach" (pp. 143-144).

Copper Antimicrobial Project

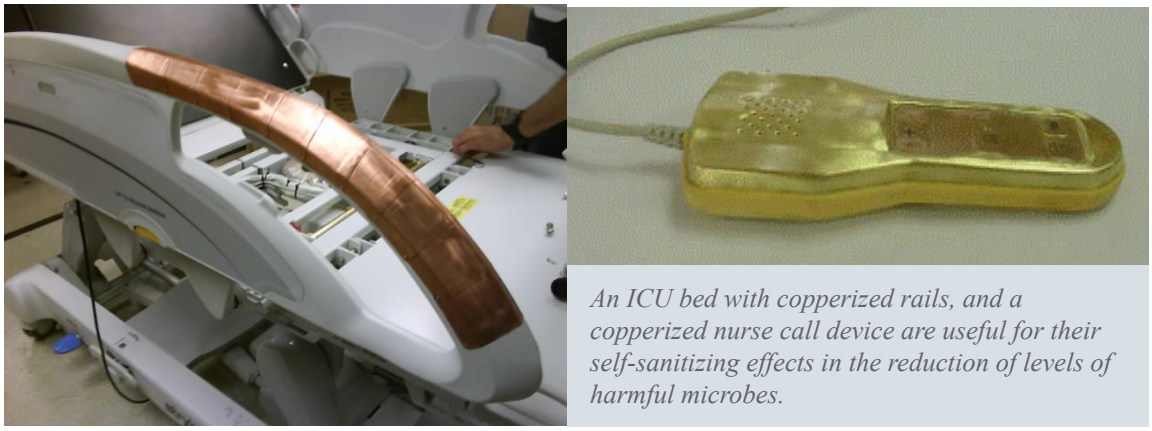
Copper Development Assoc. Inc., New York, NY

Novel Approach to Hospital Infection Control

Hospital-acquired infections (HAI) have grave consequences for patients in both military and civilian healthcare facilities. The Centers for Disease Control and Prevention (CDC) estimates that more than 2 million patients contract a hospital-acquired infection each year in the USA, resulting in nearly 90,000 deaths. In March of 2009, the CDC estimated the direct medical costs of HAIs per year in US hospitals to be $35.7B to $45.0B.

Frequently touched surfaces in healthcare facilities, such as doorknobs, push plates, bed rails, faucet handles, IV poles and others, have been found to serve as reservoirs for the spread of pathogenic microbes. Standard, CDC recommended hygienic sanitizing practices for these and other surfaces are not sufficient to eliminate these microbes. Microbes have an inherent ability to colonize on any surface and studies have also shown that these microbes can persist for days to weeks on stainless steel surfaces and polymeric materials. Microbes living on touch surfaces in hospitals frequently contaminate the hands and equipment of healthcare workers who transmit these pathogens to the patients for whom they are providing care. Infection control practices, as recommended by the CDC, have attempted to limit the spread of microbes. As with all human interventions, adherence to the recommended practices is imperfect, resulting in the spread of microbes in health care settings.

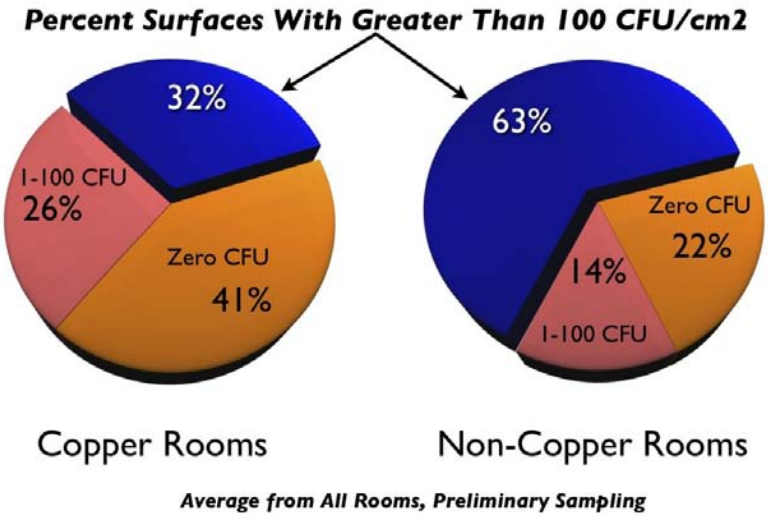
Copper and copper alloys (brasses and bronzes) have intrinsic antimicrobial properties with well documented efficacy against a wide range of pathogens, including multidrug-resistant bacteria. Research conducted under Good Laboratory Practices (GLP) conditions for the Environmental Protection Agency (EPA) has shown that within hours, copper alloys reduce pathogenic bacteria such as Methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli* O157:H7, *Pseudomonas aeruginosa,* and *Enterobacter aerogenes* by 99.9%. Other studies have demonstrated that significant reduction of bacteria such as MRSA is achieved after 30 minutes of exposure to copper alloys. Furthermore, copper has been used in hospital settings safely and effectively for more than two decades as a means to prevent the growth of *Legionella pneumophila*, the agent responsible for the pneumonias associated with Pontiac Fever or Legionnaire's disease.



An ICU bed with copperized rails, and a copperized nurse call device are useful for their self-sanitizing effects in the reduction of levels of harmful microbes.

The objectives of the Copper Touch Surfaces Program are to validate that the results observed from prior EPA and university testing are relevant in a clinical environment by demonstrating:

- Introduction of copper touch surfaces in the hospital environment will reduce the levels of harmful microbes;
- Reduction of the bioload in the hospital environment of dangerous microbes will improve clinical outcomes; and
- Self-sanitizing effects of copper will augment the CDC recommended Infection Control Program practices and thus reduce the spread of dangerous microbes and their transmission from inanimate touch surfaces to humans.



The microbial burden associated with copper surfaces was substantially lower than the non-copper counterparts.

This project is conducting a multi-year study to determine the impact of copper touch surfaces on three organisms: MRSA; vancomycin-resistant *Enterococci* (VRE); and *Acinetobacter baumannii*. This study includes multi-center clinical trials that focus on three different patient populations. The first trial will be conducted in an ICU at three hospital sites; the second clinical trial will examine the effect of copper touch surfaces in Cancer Care Units at two hospital sites; and the final trial will examine whether the intervention also is efficacious for "routine" patients, i.e., those hospitalized on a Gastrointestinal Care Unit (regular) medical ward at a single hospital site. Collaborators on this project are Medical University of South Carolina (MUSC), Memorial Sloan-Kettering Cancer Center, and Charleston Research Institute at the Ralph H. Johnson VA Medical Center.

Preliminary results of the first study indicate that of all the surfaces tested, the bed rails consistently showed the highest concentrations of these two microbes. The inherent microbial burden was determined by sampling six objects that would likely be coincidentally touched by patients, healthcare workers and visitors in the intensive care units at three hospitals. Microbial burden samples have been collected and processed for the equivalent of 149 weeks from a total of 692 rooms or 7599 surfaces. All objects sampled revealed concentrations of MRSA and VRE, two potentially deadly microbes that represent a risk to patients, healthcare workers, and visitors.

Fabrication of the copper components and the installation of the objects in the ICUs were recently completed. Preliminary results are encouraging. The microbial burden associated with the copper surfaces was substantially lower than the non-copper counterparts in the rooms studied. Sixty-seven percent of the copper objects were found to have fewer than 100 cfu/100 cm^2 while an almost inverse relationship was observed for the non-copper objects, where greater than 63% of the objects evaluated were found to have a microbial burden greater than 100 cfu/100 cm^2.

Copper Antimicrobial Project in the News

Killer Copper May be Just What the Doctor Ordered. American Metals Market, June 1, 2008.

Copper Fights Hospital Infections. Ivanhoe Medical Breakthroughs, August 1, 2008 www.ivanhoe.com.

Armed with Copper, Researchers Attacking Hospital Infections. Newark Star Ledger, August 28, 2007.

Andy Kireta Sr. – President, Copper Development Association. "Collaboration Now" interview on CNBC, November 2008.

Dr. Michael Schmidt National Public Radio's "Science Fridays" interview titled Watch Out Bacteria: Copper Kills Germs, January 16, 2009.

Portable X-ray Project

General Electric Global Research
Niskayuna, NY

Improving the Quality of Forward-Deployed Medical Imaging

Delivering continuity of care to forward-deployed personnel is of critical importance. In the late 1990s, the armed forces initiated a program to reconfigure battlefield medical support functions, and Air Force Expeditionary Medical Support units were equipped with lightweight, compact diagnostic x-ray equipment to advance the deployability of these systems and the care they provide. The military continues to seek ways to improve the level of radiography care it offers to forward-serving battlefield forces. Rapidly deployed mobile x-ray systems allow military medical personnel to provide prompt "on-site" diagnosis of battlefield related injuries facilitating immediate treatment. Imaging capabilities are present in combat-support facilities today. Currently available rapidly deployable mobile diagnostic x-ray systems for military applications are based solely on film-screen or computed radiography (CR). Although thin, rugged, and lightweight, film and CR are inferior to their digital radiography (DR) counterparts due to decreased image quality, reduced patient throughput, and delays in diagnosis resulting from film-screen development or CR phosphor plate readout requirements. The addition of ultra-portable diagnostic imaging immediately available at the bedside will further enable rapid treatment and the transmission of high-quality images to remote radiologists to improve the treatment of battlefield injuries.

Engineers at GE Global Research, collaborating with research scientists at Emory University and TATRC are working to incorporate the advanced diagnostic image quality of GE Flat panel digital detector technology in portable x-ray systems. In the late 1990s a prototype was developed to transform a 41 cm detector from the fixed configuration found in hospital imaging wards to a portable, tethered detector that could bring technology to the ER and the ICU wards. The technical developments from this program were the basis for the GE Healthcare Definium AMX 700, which can be found in hospitals today.

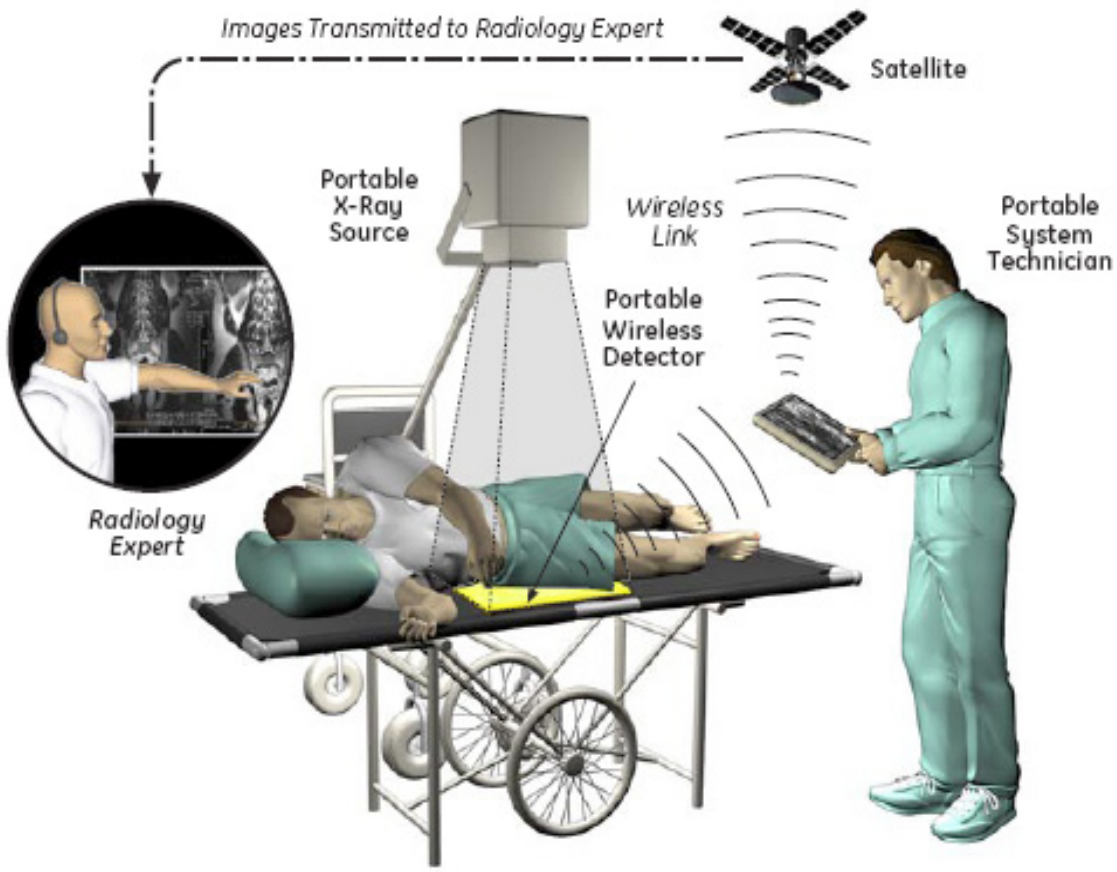
While the tethered detector was a development that made x-ray capabilities available to ER and ICU wards, operation without the tether will pave the way for battlefield applications. GE has executed programs, in conjunction with TATRC surveying existing wireless technology to determine if data throughput requirements can be met without a wired connection, and to design a rugged, forward-field deployable digital radiography system that will provide diagnostic image quality at the bed of injured personnel and to remotely located experts.

GE's Six Sigma approach was used for the design. The Six Sigma approach is a customer-focused, data-driven philosophy that enables product design and processes to meet the end-user expectations with high quality levels. A critical piece of this approach is a process to capture and establish customer requirements through an exercise called "Quality Flowdown." GE Researchers, along with TATRC personnel, spent several days at Ft. Lewis, WA working with military stakeholders to carry out the critical "customer input" phase of this process. Military participants included active and retired military personnel, the majority of whom had deployed and recently returned from the theater of operations on the battlefield. Included in this group are Radiologists, Staff Sergeants, Specialists, and Physicists. All were willing and eager to frame requirements for a forward-deployed portable x-ray system. The key high-level system characteristics gathered in this exercise were classified into seven major categories; Availability, Transportability, Durability, Reliability, Portability, Flexibility and, Simplicity.

These high-level customer requirements were transformed into concrete specifications and further characterized by the GE team into specific sub-system capabilities. It was clear from the resulting

GE PORTABLE X-RAY FAST FACTS FY08 - FY10

- 3 Projects
- 5 Patents
- 2 Provisional Patent Applications



The Next Generation Portable X-ray will allow for technicians on the front lines to remotely image a wounded Warfighter, and transmit those images to a radiology expert at the nearest trauma hospital allowing for faster diagnosis and triage.

detector subsystem requirements that the digital detector with its glass panel and sensitive hardware required significant development effort. Modeling of mechanical packaging options gives us a design that will meet the rugged requirements, the addition of the wireless and battery operation will free the detector of its tether and a custom positioner design with provide the flexibility required for tube positioning and imaging applications without the weight and space necessary for systems found in brick and mortar facilities.

Currently a prototype is being developed to demonstrate the design presented to and accepted by the military stakeholders. Key areas of focus of the prototype development are the detector ruggedization, wireless integration, and development of a system that can be easily transported to combat support hospitals in theater and survive the environment there. This will be further developed with the assistance of the US Army Medical Materiel Agency (USAMMA) portfolio managers.

GE Portable X-ray Representative Publication

Sechopolus I, Eberhard JW, Schmitz A, "A Fast and Simple Software-Based Method for XRay Scatter Reduction in Portable X-Ray Systems." *Med Phys.* 2008; 35: 2663.

Health Disparities Projects

University of South Carolina, Columbia, SC

Health disparities are differences in the incidence, prevalence, mortality, and burden of diseases and other adverse health conditions that exist among specific population groups in the United States. Studies have shown that despite the steady improvements in the overall health of the United States, racial and ethnic minorities experience a lower quality of health services, are less likely to receive routine medical procedures, and have higher rates of morbidity and mortality than non-minorities.

TATRC is an active member of the Federal Interagency Management Team (FIMT), supporting the National Partnership for Action (NPA) to end health disparities, a program sponsored by the Department of Health and Human Services.

"This multi-investigative research effort has significant public health implications for both the military and civilian populations."

Dr. Saundra Glover
Institute Director and Principal Investigator
Health Disparities Project

Soldier Health Promotion to Examine and Reduce Health Disparities (SHPERHD)

The University of South Carolina (USC)-Institute for Partnerships to Eliminate Health Disparities (IPEHD) has secured a cooperative agreement with TATRC through a DoD effort to address disparate health issues at the nation's largest Army training activity, Ft. Jackson, SC.

This project examines the root causes of military attrition and many of the factors that contribute to Soldier health issues (diet, military environment, physical activity patterns, physical readiness, stressors and anxiety), both pre- and post-deployment. A key area of focus will be PTSD and mental health.

Phase I of the project brings together several USC researchers with expertise in nutrition and diet intervention, physical fitness and musculoskeletal injuries, athletic training, and mental health research. The primary objectives are to assess baseline data of military personnel at key stages of recruitment through basic combat training to better develop the appropriate interventions to reduce attrition.

Ft. Jackson is the US Army Basic Combat Training Center of Excellence (USABCTCoE), through which the Experimentation and Analysis Element (EAE) has a primary goal of linking training and research communities to better formulate research studies. Joint Initial Military Training (IMT) workshops facilitate research discussions among representatives from other military installations such as Ft. Sill, Ft. Benning, and Ft. Leonard Wood, in addition to military personnel from the US Army Center for Health Promotion and Preventive Medicine (USACHPPM), and TATRC.

Dr. Saundra Glover leads the investigative team. The co-investigative team includes Dr. Sonya Jones, Dr. Mark Davis, Dr. James Mensch, and Dr. Shawn Youngstedt. To optimize research findings and develop the most appropriate interventions, each project lead is paired with a member of the EAE research staff at Ft. Jackson. The EAE staff, LTC Sonya J. Cable, Dr. Kelly Williams, and Dr. Stephanie Muraca, will work with each of the respective investigators to refine the research design and establish the most relevant work plan and project interventions.

"This community-based research project affords a tremendous opportunity to continue shaping the training environment with science." says LTC Cable, Director of the EAE, USABCTCoE, and Ft. Jackson site principal investigator.

This project will provide a framework for understanding the historical and cultural backgrounds of Soldiers, and how certain factors (poverty, educational history, inequities in healthcare access, diet, mental health) contribute to health disparities.

Project 1 is focused on obesity and nutrition issues. This will include evaluation of the Physical Training (PT) program; assessment of whether obesity de-motivates Soldiers; and drill sergeant knowledge of nutrition/obesity issues. A primary interest will be the "life course perspective" (impact on Soldier entrance into the military environment) in order to better understand the transition.

Project 2 will assess the baseline data for injury rates and examine the training regimen (load and progression) during basic combat training (BCT), with the recommendation of Ft. Jackson personnel. The Certified Athletic Trainer-Forward (ATF) program collaborates with on-site certified athletic trainers to analyze data related to lost hours from training, Troop Medical Center visits, heat-related injuries and Army Physical Fitness Test scores.

Project 3 examines the methods for screening recruits for mental health problems (such as PTSD) at point of intake; stigma associated with seeking mental health services; the career path of Soldiers; the small number of mental health referrals; and the impact of sleep deprivation on mental health (also a factor in Soldier injury).

Health Equity and Wellness Project

This project will address the disproportionate burden of chronic diseases by implementing a series of community based research and services outreach initiatives designed to reduce the burden of diseases that prevent enlistment into the armed forces and/or reduce the functional tenure of active duty military personnel. These same diseases also place an inordinate burden on retired military personnel, Veterans and military dependents. TATRC will partner with Dr. Sabra Slaughter, Associate Professor at the Medical University of South Carolina (MUSC), to address some of these critical unmet health care needs through medical research, while also evaluating the impact on racial, ethnic and socioeconomic groups with reference to health status and access to care.

MUSC has a long-standing history of addressing health care disparities through design, implementation, and coordination of a number of the NIH-supported research centers and initiatives. The goal of this proposed research is to ensure a military-ready population that is healthy, and to reduce the health risk factors that prevent military enlistment or retention while on active duty.

The researchers at MUSC seek to increase the awareness of the burden of chronic disease in the southeastern region; to develop novel methods to engage communities in the prevention and treatment of chronic diseases; to develop community based services and research initiatives focused on chronic diseases and socioeconomic factors that prevent military enlistment or reduce the functional tenure of active duty military personnel; and to develop youth-based, active and interactive, electronic modalities to increase the prevention, detection and treatment of chronic diseases, as well to improve compliance with preventive and treatment strategies.

Health Disparities Related Publications

National Partnership for Action to End Health Disparities. US Dept. of Health and Human Services. "The National Plan for Action Championing Outcomes - Achieving Health Equity. http://minorityhealth.hhs.gov/npa Dec 31, 2009.

Glover S. H., Xirasagar, S., Jean, Y., Pastides, H. Academic Partnerships with Historically Black Colleges and Universities: A public health professions project. *J Health Care Poor Underserved*. 2009; 20: 18-28.

Egede L., Boxworth H., The Future of Health Desparities Research: 2008 and Beyond. *J Gen Int Med*. 2008; 23: 706-708.

Hibernation Genomics (HG)

Institute of Arctic Biology, University of Alaska at Fairbanks Fairbanks, AK

Mechanisms for Metabolic Suppression and Neural Protection

The research at the University of Alaska (U of A) at Fairbanks is leveraging the new understanding of how mammalian extremophiles like the Arctic Ground Squirrel (AGS) and the Black Bear have adapted to the harsh winter conditions. The overall goal of their research program is to understand the fundamental molecular and biological adaptations that create the animals' unique capabilities. Understanding such mechanisms can identify unique solutions to the difficult medical problems that are associated with battlefield trauma, both acute survival following traumatic hemorrhage and improved recovery/rehabilitation.

Setting traps for Arctic Ground Squirrels in northern Alaska.

Surviving Hemorrhagic Shock (HS) and Cardiac Arrest- A novel AGS model

In a recent series of studies it has been demonstrated that the AGS even when not hibernating is unique in its ability to resist 10 minutes of cardiac arrest, a period of cardiac arrest that is fatal to rats exposed to the same duration. The extent of this resistance is unknown. It is clear that the animals not only survive the period of cardiac arrest, the heart does not appear to be damaged, and other organs that were exposed to ischemia, hypoperfusion/stasis, and metabolic stress did not shut down or cease to function. The understanding of the basic molecular biology of this unique physiological adaptation is currently underway using proteomic, metabolomic and genomic discovery techniques that have been developed at U of A for the AGS.

Initial AGS genomic comparisons and bioinformatics analysis were conducted in collaboration Dr. Jun Yan, Chinese Academy of Sciences. Protein expression throughout the torpor-arousal cycle during hibernation in AGSs was analyzed. The team identified more than 3,000 unique proteins from an AGS liver. Proteins involved in protein translation and degradation, mRNA processing, and oxidative phosphorylation were significantly over-expressed in early aroused animals compared to late torpid animals. The results suggest that there is substantial post-transcriptional regulation of proteins during torpor-arousal cycles of hibernation, and may identify potential molecular targets for drug development.

Based on the dramatic difference in sensitivity of the AGS to cardiac arrest, compared to the rat, the group has begun research to characterize the potential resistance of the AGS to HS. HS is more relevant to battlefield mortality and morbidity associated with multi-organ failure than cardiac arrest. If, as anticipated, the AGS proves to be as resistant to HS, subsequent research will investigate how to translate this resistance to non-hibernating AGS towards the long-term goal of producing treatments that will significantly enhance survivability of the Warfighter following battlefield injury.

HG FAST FACTS FY08 - FY09

- 4 Projects
- 22 Publications
- 14 PI's
- 9 Invited International Presentations
- 10 Graduate Students Trained

Understanding Black Bear Hibernation Physiology to Develop Novel Treatments for Bone and Muscle Following Traumatic Injury

Extremity injuries that necessitate extended bed-rest and immobilization of the limb for an extensive period of time can cause serious muscle and bone atrophy for combat casualty and civilian trauma patients. For Wounded Warriors, these decreases in strength of muscle and bone can delay limb recovery/rehabilitation and significantly increase the return to duty time.

Bears go through long periods (6-7 months) of hibernation and immobility without loss of muscle mass, through protein recycling and the almost exclusive metabolism of fat. Humans at bed-rest for a comparable period of time will lose 90% of their muscle strength and have significant bone loss. Bone demineralization as a result of bed-rest or loss of gravitational force is also an important issue faced by NASA in the Mission to Mars, and may benefit from the results of this research.

Unique molecular genetic resources have been created to accomplish the long-term goals of this program and to enable investigations of the molecular mechanisms that underlie natural protection in muscle and bone from disuse atrophy in human-sized (Black Bear) mammalian hibernators.

The team, collected cDNA expressed sequences tags (ESTs) representing 17,673 unique transcripts for the black bear. These sequence data and clone collection represent genomic resources are available for the broad scientific community in The Black Bear Gene Index data base (http://compbio.dfci.harvard.edu/tgi/cgi-bin/tgi/gimain.pl?gudb=bear) for functional and comparative genomics in new non model mammalian species. The Black Bear Gene Index was created in collaboration Dr. John Quackenbush, the Computational Biology and Functional Genomics Laboratory at the Dana-Farber Cancer Institute and Harvard School of Public Health. A set of ESTs representing 12,800 different genes was printed on the bear cDNA array with microarray fabrication and hybridization experiments conducted in collaboration with Dr. Louse Showe of The Wistar Institute.

A pathway analysis of results from the first bear microarray experiments showed a significant enrichment of the protein biosynthesis category by over-expressed genes in liver, heart and skeletal muscle comparing hibernating to summer animals. This finding suggests an adaptive mechanism that contributes into unique ability to reduce muscle atrophy over prolonged periods of immobility during hibernation. The list of differentially expressed genes, proteins and their associated pathways generates potential therapeutic targets towards preventing muscle disuse atrophy and osteoporosis after prolonged periods of immobilization in humans. The research team has also collected cDNA expressed sequences tags ESTs representing 13,273 unique transcripts for the arctic ground squirrel, and a set of ESTs representing 9,600 different genes was printed on the AGS microarray.

Expression profiles in bears and small mammalian hibernators shows a trend during hibernation that includes induction of genes involved in lipid metabolism and carbohydrate synthesis and depression of genes involved in the urea cycle in liver. Leveraging the results of these studies could translate to novel approaches to improve recovery from traumatic injury to muscle and bone. The results of these studies are being coordinated with the R&D efforts in DoD and other government agencies.

Hibernation Genomics Representative Publications

Fedorov VB, Goropashnaya AV, Tøien Ø, Stewart NC, Gracey AY, Chang C, Qin S, Pertea G, Quackenbush J, Showe LC, Showe MK, Boyer BB and Barnes BM. Elevated expression of protein biosynthesis genes in liver and muscle of hibernating black bears (*Ursus americanus*). *Physiol Genomics*. 2009; 37: 108-118.

Orr AL, Lohse LA, Drew KL, Hermes-Lima MH, Physiological oxidative stress after arousal from hibernation in Arctic ground squirrel. *Comp Biochem Physiol A Mol Integr Physiol*. 2009; 2: 213-21.

Su B, Wang X, Drew KL, Perry G, Smith MA, Zhu X, Physiological Regulation of Tau Phosphorylation during Hibernation. *J. Neurochem*. 2008; 105: 2098-2108.

Yan J, Barnes BM, Kohl F, and Marr TG. Modulation of gene expression in hibernating arctic ground squirrels. Physiol Genomics. 2008; 32: 170-181.

Hospital of the Future (HOF)

Development of open, interoperable medical cyber-physical systems

The Hospital of the Future initiative was led by Amy Nyswaner, with significant contributions from Dr. Stephen Schimpf, University of Maryland Medical School. Others, notably Dr. Julian Goldman, continued to contribute as significant leaders in this important, helping to guide national programs in the area of patient safety, interoperability, and integrated clinical environment. This section describes the TATRC-facilitated research at CIMIT, Brigham and Women's Hospital, and the Vanderbilt University School of Medicine, and the interplay with the DoD Patient Safety Program, the US Army Health Facilities Planning Agency (HFPA), and the Telerobotics and Advanced Minimally Invasive Surgery (TAMIS) Center at USUHS.

CIMIT HOF

CIMIT has actively pursued how to develop and test new designs, processes and technologies that move the hospital of today to the hospital of tomorrow. The Clinical Systems Innovation Program at CIMIT is the hub of this endeavor, and supports the efforts of the Operating Room of the Future, Medical Device Plug-n-Play Interoperability, the Advanced Imaging Procedure Room, the Neonatal ICU, the Emergency Department, the Ambulatory Practice, and the Home of the Future.

The hallmark of this work was the Massachusetts General Hospital (MGH) Operating Room of the Future. This effort, driven by the clinical community to focus on real problems, was also one that recognized the value of interdisciplinary participation and involvement. The problems were inefficient patient flow, ineffective integration and placement of numerous devices, lack of real-time data available to the team, and significant wasted down time between cases. The room, opened in 2002, focused on using the concepts of industry parallel processing as compared to the usual medical serial processing to decrease down time; creating a dashboard available to the entire surgical team with integrated data regarding the patient's history, in-room clinicians physiological measures, and surgical progress; and using RFIDs to track people and equipment. Ten industry partners participated in and committed to the design and development of the room and its technologies,

Operating Room of the Future at Massachusetts General Hospital.

"Miscommunications are a major source of errors in healthcare. We are studying the effects on patient safety and physician work processes of implementing a Comprehensive Handoff Program. The program involves two major elements: 1) training resident-physicians in teamwork principles and the standardized transmission of verbal information; 2) implementation of a computerized handoff tool that automatically imports key patient information and structures handoffs of written information.

along with the interdisciplinary team at MGH.

The concept was to develop a living laboratory inside an existing fast-paced, large surgical service, where new processes, designs and technologies could be developed and tested, prior to dissemination across the institution, or other medical centers. In this room, a minimally invasive surgeon can now routinely perform seven to eight cases a day, as compared to four to five in a comparable room with the old design and technologies; and testing of real-time alerts to anesthetists regarding documentation of allergies, and identification of aberrant blood pressure measures also takes place.

Amy Nyswaner (Center) is the TATRC lead for HOF, pictured here with Nita Grimsley (l) and Rebecca Duve (r).

Another important secondary benefit of this effort is the now national effort to lead in the evaluation and adoption of open standards and technology for networking medical devices. This effort includes involvement of the FDA, DoD, industry, and clinicians.

Subsequent Surgical Learning Laboratory efforts now include development of an Advanced Procedure Room for thoracic surgery at the Brigham and Women's Hospital (BWH), and the Advanced Multi-Modality Image Guided Operating Room at BWH. Each of these has resulted in improved care and efficiency in the room design, and has also served as a valuable information base for the design of multiple new operating rooms, not only locally but nationally.

The Emergency Room of the Future has focused on the use of new technologies and processes to more efficiently triage incoming patients, monitor the health status of waiting patients in real-time, and provide the ability to quickly locate patients whose condition worsens.

The Ambulatory Practice of the Future has a mission to design a new outpatient practice that traverses the walls of the usual physician practice, and allows for delivery of ideal care in the ideal environment. This includes home monitoring and off-site communication with the primary care physician and team, as well as new design of the office space. The new office space is scheduled to open in March, 2010.

The Home of the Future includes works to collaborate with industry to develop methods of increased independence for those needing assistance in the home.

All these efforts, though divided by work groups, lead to the ultimate vision for healthcare delivery in the future—with increased transparency and synchrony, regardless of the location of the person needing care, or the provider delivering the care.

Brigham HOF

The DoD and the Joint Commission on the Accreditation of Healthcare Organizations have found communication errors to be a contributing cause of approximately two out of every three reported

We are measuring the effects of the program on safety at Walter Reed and Madigan Army Medical Centers, and hope that the lessons learned will help to design safer healthcare systems both within and outside of the DoD."

Christopher P. Landrigan MD
MPH Director, Sleep and Patient Safe Program
Brigham and Women's Hospital

The new Ft. Belvoir Community Hospital.

sentinel events in hospitals. The handoff of clinical responsibility between medical providers is a vulnerable source of communication failure. Although handoffs between residents have become increasingly frequent in the wake of work hour reductions, standardized handoff programs have not been established in most medical centers, and most residency programs do not provide formal training in handoff skills. Furthermore, despite the known potential of technological tools such as computerized order entry to reduce medical errors, very few handoff programs import medical information directly from the patient record.

To address these concerns, researchers at Brigham and Women's Hospital are in the process of working with physicians and researchers at WRAMC and Madigan Army Medical Center to implement a Comprehensive Handoff Program. The program consists of the provision of training in teamwork and best handoff practices for resident-physicians, implementation of standardized verbal handoff procedures, and implementation of a new computerized tool that is linked to the electronic medical record. The computerized tool continuously imports data on patient demographics, allergies, medications, recent laboratories, and other clinical data, integrating them with structured patient sign-out information provided by the care team.

The goal is to decrease medical errors, improve resident communication, and improve resident workflow and satisfaction. The investigators are measuring the effects of the program using a confidential, established methodology for the collection of data on patient safety, direct observation of resident handoffs, resident surveys, and direct measurement of resident workflow using time-motion studies. If the program is successful, the investigators will work with the DoD to aid in the dissemination of the program and improvement of handoff processes throughout the military healthcare system.

DoD Patient Safety Program

TATRC and the DoD Patient Safety Program have engaged in a valuable collaboration to address and promote patient safety in military and civilian healthcare. Patient safety issues are assessed and needs that can be addresses with advanced technology are determined to ensure a safe Hospital of the Future.

Members of the DoD Patient Safety Program provide valuable subject matter expert guidance on potential and current TATRC projects in patient safety. In return, TATRC managers keep the DoD Patient Safety Program informed on emerging technologies. Through this partnership key projects are identified that would benefit military and civilian healthcare. To date these efforts have authored SBIR topics which have developed into projects that seek to improve the safety of our medication ordering, dispensing, and administering system.

According the Joint Commission root cause analysis of sentinel events, the primary causal factor (66%) of errors is inadequate communication. In an attempt to address this issue, TATRC and the DoD Patient Safety Program foster projects that promote teamwork, skills development, and technologies to assist in improved communication among caregivers. The goal is to identify systematic approaches to ensure safe and reliable care for all military and civilian patients.

HFPA/TATRC Collaboration

TATRC and the Army's HFPA have engaged in a valuable collaborative effort to provide the best health care to our Warfighters and their families. This relationship enabled both organizations to learn from one another sharing knowledge and developing plans to meet these combined goals.

HFPA has been able to incorporate elements of the Operating Room of the Future concept into the

new hospital construction projects totaling over $2.5B. Other components within "Of the Future" healthcare delivery models being incorporated into the Army's medical facilities include Emergency Department and Ambulatory Care. By adding requirements for interoperability and the integration of technology systems into contract language and requests for proposals, TATRC emphasizes the requirement for an open standards provisioning for seamless systems in the future. Forward planning means the inclusion of spaces for medical simulation training rooms in MTFs—for healthcare provider critical skill maintenance, credentialing and certification. Ambulatory check-in kiosks are being designed into new buildings along with trials to determine staff efficiency, patient throughput, and outcomes. New waste disposal technologies are also being planned for testing in 2010. Projects for which we are incorporating these elements include; Forts Benning, Hood, Carson, Belvoir, Bragg, Riley, and Bliss, to name a few.

HFPA continues to collaborate with TATRC and the DoD Patient Safety Program to address strategic goals to impact patient safety with facility and technology solutions.

TAMIS HOF

The TAMIS program, based in the National Capital Area, is a tri-service asset that combines the resources of multiple MTFs and the USUHS. TAMIS has developed a robust telesurgical infrastructure with surgical robotic systems in both the clinical and laboratory settings. The TAMIS Training & Research Center has the only fully credentialed Robotic Surgery Training Program within the DoD.

TAMIS is currently leading efforts in operational implementation of remote, robotic surgical mentoring and has the unique ability to develop surgical simulation strategies and specifically, robotic surgical training programs into curricula for implementation into both Graduate Medical Education (GME) and Continuing Medical Education (CME) programs within the National Capital Consortium. The development of military-specific telementoring and subsequently telesurgery capabilities will allow for greater projection of scarce military expertise to remote locations and may also play a role in medical diplomacy and humanitarian assistance missions.

TAMIS operates the clinical robotic surgical services platform at WRAMC. The da Vinci® S surgical system is a tri-service asset with multi-disciplinary clinical utilization. This operating room was renovated in late 2006 to support robotic surgical procedures.

This program presents a unique DoD platform to bring advanced technology, to MTF's worldwide while providing oversight and guidance for future military programs in surgical robotics.

Vanderbilt Hospital of the Future Vigilance Surgical Safety System

Human Factors Assessment of Vigilance in the Operating Room

The primary aim of the study is to improve patient safety in the operating room (OR) by improving the means by which anesthesiologists simultaneously monitor multiple surgical cases throughout their work shifts. It is hypothesized that when anesthesiologists use the mobile Vigilance system for patient monitoring, as opposed to standard monitoring practices, they will have a higher situational awareness (SA) of clinically significant physiological events occurring in their surgical patients. Changes in provider workload, work efficiency, and clinical communication patterns are serving as secondary outcomes of the study. This initial study of the Vigilance system is focused on detecting serious deviations in heart rate, blood pressure, temperature, and blood oxygen saturation. Consenting faculty anes-

thesiologists are being randomized to either Vigilance or stand monitoring prior to their work shift. SA and mental workload are being measured by telephone surveys administered randomly during their shifts. Work efficiency is being measured and compared by observing patterns of work and communication flow of the anesthesiologists assigned to the two study arms.

Vigilance Safety System in Post Operative Patients

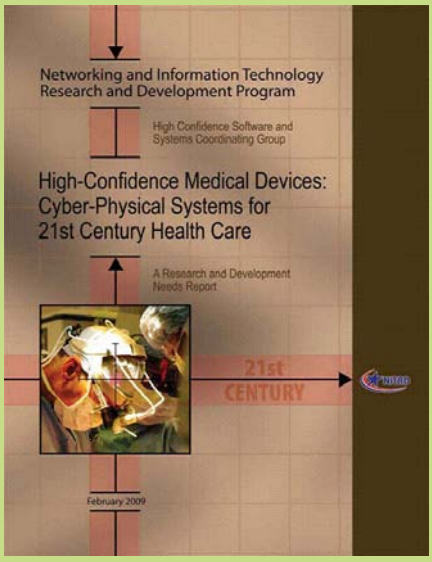
The primary aims of our second study are to implement the Vigilance Surgical Safety System architecture in a post-operative unit of the hospital and to improve the detection and communication of abnormal physiologic states of postoperative patients to members of the rapid response team (RRT). Using a randomized control trail methodology, the investigators are placing wireless physiological monitors on otherwise non-monitored postoperative orthopedic and urologic surgical patients. The Vigilance Alert Engine is used to process monitored patients' physiological data and to generate timely pager and application based alerts for RRT providers. The Vigilance system also provides the RRT providers an interface to the patient's electronic medical record in an effort data access and to improve clinical decision-making. The hypotheses are that more abnormal physiologic states will be detected earlier in patients randomized to Vigilance-monitoring than in patients randomized to routine postoperative monitoring, and that use of the system will result in earlier detection and communication to the RRT that will result in earlier implementation of corrective action and fewer codes and hospital deaths (primary outcome). In addition, it is hypothesized that Vigilance monitored patients will experience shorter ICU and hospital lengths of stay. As of August 31, 2009 over 1,000 postoperative patients have been enrolled into the study.

Medical staff inform a perioperative patient about the features and purpose of the wireless remote monitor.

"Incentives are needed to enable effective cooperation between government, industry, and academia to build the underpinning standards and networking and information technology frameworks (e.g., testbeds) for developing open, interoperable medical cyber-physical systems."

from High-Confidence Medical Devices: Cyber-Physical Systems for 21st Century Health Care. A Research and Development Needs Report. Networking and Information Technology Research and Development Program. February 2009.

http://www.nitrd.gov

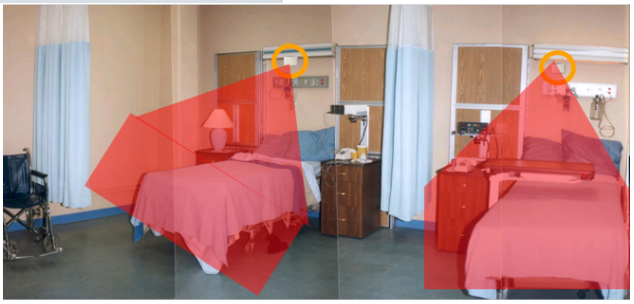


Handwashing Compliance Reminder and Documentation System

Massachusetts General Hospital, Boston, MA

A 'zone of protection' is generated for the patient through a reminder system that emits a quiet beep to the provider in the event they have not washed their hands prior to engagement with the patient. This technology can be incorporated into a clinician's or other care-giver's badge to remind them, in real time.

I.D. Badge Receiver



Protection Zone Transmitters

A Joint DoD/VA Project

Five to 10 percent of hospitalized patients develop a HAI. This represents a major health issue for DoD, VA, and civilians. The emergence of particularly virulent strains, such as MRSA and VRE, has brought this issue to the fore amongst healthcare safety concerns.

Proper hand cleansing is the most critical element to decrease HAI's, but poor compliance for hand hygiene is well documented. Expensive education and surveillance programs have only resulted in transient improvement. CIMIT's solution to this problem is to generate a 'zone of protection' for the patient through a reminder system that emits a quiet beep to the provider in the event they have not washed their hands prior to engagement with the patient. The solution further captures hand hygiene statistics for use as deemed appropriate by hospital administration. This has the potential to significantly increase patient safety and dramatically reduce costs.

CIMIT's technology can be incorporated into a care-giver's badge to remind them, in real time, if proper hand-cleansing has not occurred according to room-specific protocols. The unique features in this system will minimize disruption of clinical efficiency and facilitate compliance in a non-threatening way, yet still allow data-logging to document compliance for quality-assurance purposes. The system will detect when proper cleansing has or has not occurred, and do so in a context-sensitive manner. It will be flexible enough to conform to different care practices in different units, subtle enough to not embarrass the clinician in front of the patient, and inexpensive enough to be used by every clinician. It will be designed for quick and easy installation at the local unit level, yet will scalable, so as to not require expensive or invasive infrastructure modification or installation.

To date, a prototype device has been developed and preliminary testing has proven successful. The project was selected for funding from the DoD and VA JIF, to demonstrate how this system will work in a ward of the Boston VA Hospital and in a ward at the USAISR.

HANDWASHING FAST FACTS FY08-FY09

2 Patents Pending

3 Ongoing licensing discussions

Information on Handwashing Compliance Reminder and Documentation System

US Patent Application: Ultrasound Compliance Zone System, filed June 16, 2009.

Massachusetts Technology Transfer Center Life Sciences Innovation Day, June 3, 2009: Handwashing Compliance Reminder and Documentation System.

Fort Detrick, OASIS Demo and presentation, Handwashing Compliance Reminder and Documentation System; June 17, 2009.

Pharmacovigilance

OTSG Pharmacovigilance Center Silver Spring, MD

In FY 2009, OTSG-MEDCOM and FDA/CDER entered into a collaboration in the analysis of data for the purpose of evaluating the safety of drugs. The scope of this collaboration is documented in two interagency agreements:

- Mining Longitudinal Data for Known and Unknown Adverse Events for Support of the Pharmacovigilance Pilot (IAA Number 224-08-3014), funded by FDA at a cost of $2,025,000.
- Supplemental Staffing Resources in Support of FDA Pharmacovigilance Pilot Project Requirements (IAA Number 224-08-3015), funded by FDA at a cost of $545,000.

The overall focus of the MEDCOM-FDA collaboration is research into and development of enhancements to existing software in support of the FDA Sentinel Initiative, using data derived from DoD medical records and medical insurance claims related to its population of active service personnel, dependents, and retirees, as well as the support of supplementary staff at the OTSG Pharmacovigilance Center (PVC) to carry out medical product safety research of interest to the collaborating parties.

During the first nine months of the collaboration, the PVC has succeeded in enhancing its signal detection software and in deploying that software in a server facility to support interactive use by staff at the Pharmacovigilance Center. The mechanism for this activity was a contract with the Lincoln Safety Group at Phase Forward, Inc., and funded by MEDCOM with funds provided through the IAA. Specific technical accomplishments include:

- Establishing a production server environment supporting interactive use of the application and development of custom analyses by the PVC, and delivery of technical support and training to the PVC user community.
- Completion of two cycles of data cleaning, loading, and restructuring for analysis of the ~12 million patient DoD healthcare database, with data on enrollment, demographics, prescriptions, diagnoses, and procedures.
- Implementation of a sophisticated exposure-based signal detection and signal evaluation methodology based on the "Brown algorithm," as directed by FDA with end-user support for analysis run definition and exploration of results.
- Generation of single- and multi-patient graphical timeline drilldown displays that facilitate the examination and validation of results.
- Creation of facilities for the identification of cohorts of patients through data mining and queries (including temporal queries), and the downloading of selected information on these patients.

There remain several challenges in the evolution of the signal detection facility to a full production status. The complete set of medical data resources useful in signal detection must be assembled from multiple systems within DoD, and data elements outside the core data available from the Medical Data Repository (MDR) are still being assembled. Also, it has been difficult to provide rapid response times for some analysis tasks generated by the PVC on the large healthcare database. Further work in these areas, as well as work to improve the ease of use of the software, is continuing in the remainder of the year. Lastly, there is not enough flexibility in the software to answer the kinds of questions required for rapid analysis of signals. The Brown algorithm does not take into account switching (if a patient takes one drug and then switches to a second drug), a drug as an adverse event proxy, or temporal relationships.

PHARMACOVIGILANCE FAST FACTS FY05-FY07

5 DoD Patient Safety Alerts & Policies
CRADA Developed with eHealth
Renewal of Inter Agency Agreement
PVC Implemented for Army OTSG
DBT Certification

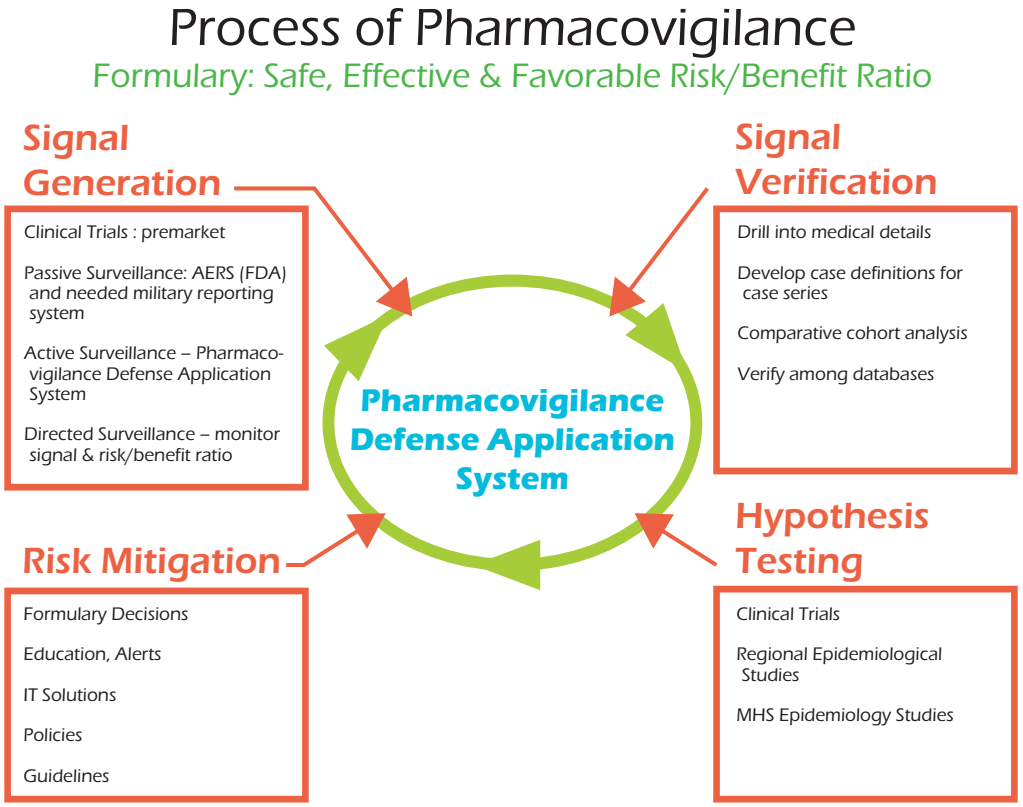
Successful Data Analysis and Accomplishments

Analysis of fentanyl compared to opioids without fentanyl. This analysis demonstrated the increase risk of fentanyl for accidental overdose.
Analysis of zonisamide and topomax demonstrated a similar risk for metabolic acidosis as reported by the FDA. This resulted in modifying CHCS to put in a comment under the drug in the CPOE that states " MONITOR BICARBONATE."
Analysis of Tamiflu demonstrated the signal for mis-prescribing the prophylactic doses to those with influenza. Coordinated with DoD Patient Safety Program to alert providers of possible signal.
Helped establish CENTCOM policy to ban use of Chantix in-theater and recommending with OTSG members not to use Zyban.
Demonstrated a signal for polypharmacy for PTSD on day of diagnosis and briefed the Surgeon General.
Helped demonstrate the mis-prescribing of mefloquine in patients with neuropsychiatric conditions. This led to policy at DoD to make doxycycline the drug of choice for prophylaxis of malaria in some regions and mefloquine to be second line.

During the first nine months of the collaboration, staff supported by the IAA at the PVC performed a number of safety analysis tasks. The mechanism for this activity was a contract with GDIT funded by DoD with funds provided through the IAA. Specific accomplishments include:

In several cases, the scientific research work performed by the PVC staff helped identify gaps in the available data and software resources and led to improvements in these resources. An extension of the collaboration for the FY 2010 year is presently under discussion between FDA and DoD.

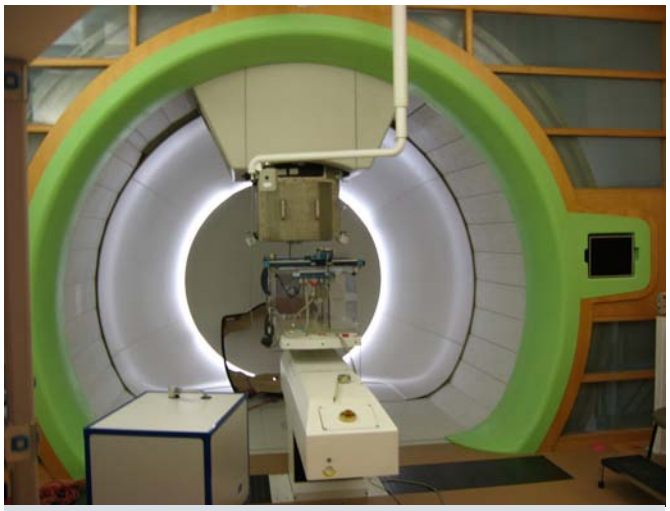
During this period, the PVC staff also found problems with the military's data dictionaries. They noted that their pharmacy data transaction system (PDTS) had inaccurate dispense dates that linked to the claims processing and not the dispensing of the medication. The PVC took these findings and requested the data warehouse (MDR) data dictionary be updated and they requested the requirements group for the new EMR pull data from the "DRX key" from the c(CHCS) for all dispensing of drugs, both new and refills. In addition, the PVC requested that the ALLERGY section be linked with the Computerized Physician Order Entry (CPOE) and that the CPOE document reasons why drugs are stopped (intolerant, ineffective, allergy, complete treatment, or patient reason). In addition, PVC documented the need for establishing an ADE reporting tool and development of an enterprise database.



Proton Beam Therapy (PBT) Technology Development

Hospital of the University of Pennsylvania, Philadelphia, PA & Loma Linda University Medical Center, Loma Linda, CA

External beam therapies (EBTs) such as Intensity Modulated Radiation Therapy are gaining wide acceptance as alternative to surgery for several cancers including lung, prostate and breast. One of the drawbacks to EBTs is that targeting of the beams can be inaccurate due to the high energy nature of the particles involved. These beams are not always absorbed by the target and can pass on to healthy tissue, causing unnecessary damage. PBT, a subset of EBT, promises to accurately deliver high-energy radiation to cancerous tissues. The tissue-proton interaction differs from x-rays or other sources of EBT radiation as the energies can be adjusted for tumor depth using a technique referred to as "Spread Out Bragg Peaks." The engineering and implementation of PBT is a major multidisciplinary challenge requiring the expertise of radiation oncologists, engineers and theoreticians. TATRC supports two unique efforts to develop this medical capability.



The future of advanced cancer treatment therapies using proton beams.

Dr. James McDonough of the Hospital of the University of Pennsylvania sees potential for this technique to save the lives of those suffering from a variety of cancers. In order to accurately control the dosimetry of the protons, Dr. McDonough has a comprehensive program to develop tools that will precisely modulate proton beams, control patient movement, monitor treatment in real-time and develop advances in three-dimensional treatment planning for PBT. He has also has engaged experts at WRAMC for expertise in radiation oncology and treatment planning.

The Loma Linda University Medical Center is the country's first proton treatment center. In the 1960s, Dr. James Slater conceived a plan to develop the core technologies needed for such a clinic. The facility went online in the early 1990s. In order to revolutionize the current standard of care for PBT, Dr. Slater and his team partnered with TATRC to manage the resources needed to develop innovations in active beam scanning (ABS) technologies. Previous efforts funded by TATRC completed the accelerator and beam transport system's enhanced control system. This provided the foundation for delivering ABS to the treatment rooms; increased dose monitoring sampling and accelerator cycle delivery; and decreased fluence variation. These are critical factors for targeting irregularly shaped volumes common in cancers and other diseases. The innovations of both of these organizations have put forward the next-generation of technologies that will ensure the availability of high-quality, less-invasive cancer therapy.

Proton Beam Publications

Belard, A., Tinnel, B., Wilson, S., Ferro, R., O'Connell, J. Development of a Remote Proton Radiation Therapy Solution over Internet2. *Telemed e-Health*. 2009; 15: 998-1004.

McDonough J. Tinel B. The University of Pennsylvania/ Walter Reed Army Medical Center proton therapy program. *Technology in Cancer Res Treat*. 2007; 6: 73-6.

Bush DA, Slater JD, Garberoglio C, Yuh G, Hocko JM, Slater JM. A technique of partial breast irradiation utilizing proton beam radiotherapy: comparison with conformal x-ray therapy. *Cancer J*. 2007; 13: 114-8.

PROTON BEAM FAST FACTS FY03 - FY08

Total funding $39,645,997

3 clinical trials scheduled to begin in 2010

2 separate projects/institutions

Virtual Humans

Institute for Creative Technologies
University of Southern California
Marina del Rey, CA

Revolutionizing Health Risk Communications

Disseminating healthcare information to Warfighters and their families is a persistent and growing problem. Although medical information is increasingly available over the web, users can find this overwhelming, contradictory, and impersonal. SimCoach proposes to build on advances in "human-centered" computing to create a more personal, reassuring and, ultimately, more effective interface for access and dissemination of medically relevant information.

The need for military-specific health information is growing at an astounding rate. In spite of a Herculean effort on the part of the DoD to produce and disseminate behavioral health programs for military personnel and their families, the complexity of the issues involved continue to challenge the best efforts of military mental health care experts, administrators and providers.

A February 2007 report from the "American Psychological Association Presidential Task Force on Military Deployment Services for Youth, Families and Service Members" described three primary barriers to military mental health treatment for both active duty members and families: availability, acceptability and accessibility. While advances in technology have begun to show promise for the creation of new and effective clinical assessment and treatment approaches, from Virtual Reality to computerized prosthetics, improvements in the military health care dissemination/delivery system is required to take full advantage of these evolving treatment methodologies, as well as for standard proven intervention options.

The Institute of Creative Technology (ICT) is developing an intelligent, interactive program called "SimCoach" to help Warfighters and their families initiate the medical treatment process and to learn about resources for psychological health and TBI.

Through SimCoach, rather than a traditional web portal, Warfighters, spouses, or other family members will be able to initiate a dialogue about their medical concerns with an interactive Virtual Human (VH). This intelligent graphical character will use speech, gesture, and emotion to introduce the capabilities of the system; solicit basic anonymous background questions about the user's history and

Virtual characters developed by ICT for various Army training applications.

"By leveraging artificial intelligence, voice recognition, videogame and avatar interaction technologies, SimCoach will provide Warriors with private, virtual access to psychological health and TBI resources."

BG Loree Sutton, M.D.
Director, DCoE for PH and TBI

The Stability and Support Operations (SASO) application uses virtual humans in an advanced multi-agent system, which integrates speech recognition, natural language processing, dialogue management, task modeling, emotional modeling, and nonverbal behavior for trainees to develop negotiating skills.

SGT Star, a virtual human prototype, answers questions for potential Army recruits through an artifical intelligence program.

medical concerns; and direct them to appropriate medical information and medical professionals.

Users interact with this character by typing, clicking on character-generated menu options and some limited speech interaction during the initial phases of development. The feasibility of expanding this to full spoken interaction will be explored in the later stages of the project. VH appearance, behavior, and dialogue will be designed to maximize user comfort and satisfaction, but also facilitate fluid and truthful disclosure of medically relevant information. Based on the issues delineated in the initial interview, the user will be given access to a variety of general relevant information on psychology, neurology, rehabilitation, the military healthcare system, and also to other Service Members. They can also be directed to experts on specific areas such as stress, brain injury, marriage counseling, suicide, rehabilitation, reintegration and other relevant specialties. The user can progress through the system at their own pace over days or even weeks as they feel comfortable and the VH will also be capable of "remembering" the information acquired from the previous visits and build on that information in similar fashion to that of a growing human relationship. Interspersed in the program would be the option to allow the user to perform some simple neurocognitive and psychological testing to inform decisions on initial referral options. Users will also have the option to print out a summary of the computerized sessions to bring with them when seeking medical treatment to enhance their comfort level, armed with knowledge, when dealing with the "real" human clinical care providers and experts.

SimCoach is not conceived to deliver treatment or diagnosis or to replace human providers and experts or seen as a replacement for existing services. Instead, SimCoach will aim to start the process of engaging the Warfighter and/or their family to become aware of and to seek out treatment programs, to give advice and encouragement, and act as a supplement that will allow individuals to initiate treatment who may otherwise be initially uncomfortable talking to a "live" person. Successful execution of this project would likely drive the state-of-the-art in similar domains of civilian healthcare.

Virtual Humans Publications

Kenny PG, Parsons TD, Gratch J, Rizzo AA. Evaluation of novice and expert interpersonal interaction skills and a virtual patient. "Intelligent Virtual Agents." Berlin: Springer Verlag, 2009; 511-12.

Kenny PG, Parsons TD, Gratch J, Rizzo AA. Virtual humans for assisted health care. Proceedings of the 1st International Conference on Pervasive Technologies Related to Assistive Environments (PETRA). 2008; 282: 1-4.

Kenny PG, Parsons TD, Rizzo AA. Human computer interaction in virtual standardized patient systems. Human-Computer Interaction. "Interacting in Various Domains." Berlin: Springer Verlag, 2009; 514-23.

Parsons TD, Kenny P, Cosand L, Iyer A, Courtney C, Rizzo AA. A virtual human agent for assessing bias in novice therapists. *Medicine Meets Virtual Reality.* 2009; 17: 253-258.

Kenny PG, Parsons TD, Pataki CS, Pato MT, St-George C, Sugar J, AA Rizzo. Virtual Justina: a PTSD virtual patient for clinical classroom training. *Ann Rev Cybertherapy Telemed.* 2008; 6: 113-118.

Video Laryngoscope

Omaha VAMC, Department of Anesthesiology, Omaha, NE

Video Laryngoscope Blade and the Boedeker Intubating Forceps for Airway Management

Since 2006, TATRC has been supporting efforts led by Dr. Ben Boedeker to develop increasingly improved airway management tools for the far forward battlefield. This effort has been centered around video laryngoscopy. With the advent of video laryngoscopy, a need for novel support devices was created. Two novel support devices, an intubating forceps and the suction video laryngoscope blade were developed with TATRC augmentation funding support and fielded for military use. These devices are described in this report.

Airway management is a cornerstone of trauma management. Intubation is often necessary for patients with severe trauma to secure an open airway. This placement of an airway is achieved by direct visualization through the mouth. Performing the procedure has traditionally been challenging to accomplish in a patient with a small mouth, large tongue, small jaw bone or in the presence of neck trauma. Video laryngoscopy facilitates the accomplishment of the procedure by using a camera on the distal tip of a traditional video laryngoscope to allow "seeing around the corner" and visualizing the critical opening. When using standard laryngoscopy and a direct line of sight, a 10-degree view is usually achieved of the opening compared to a 60-degree view with a video laryngoscope. To use video laryngoscopy effectively, new instruments are necessary. A suction capable video laryngoscope blade and compatible retrieval forceps allows for rapid clearance of secretions, blood, and debris from the visual field of trauma victims undergoing field intubation using indirect video laryngoscopy. The novel curved intubating forceps' reach extends into

Completed Phases and Accomplishments for the Suction Video Laryngoscope Blade

1: Develop specifications for and initial prototypes of an indirect video laryngoscope blade with an integrated suction channel that allows use of a coupled medical suction apparatus to clear body fluids from the pharynx.
A prototype video laryngoscope blade with integrated suction channel was created at the Center for Advanced Technology and Telemedicine, UNMC/Omaha VAMC, Omaha NE and evaluated by Dr. Boedeker on a hemorrhagic airway simulator developed by the Center for Advanced Technology and Telemedicine. A final working prototype blade was created by Karl Storz Endoscopy Inc and tested.

2: Conduct iterative evaluation of design and functional characteristics of the initial prototype video laryngoscope blade with an integrated suction channel.
Our laboratory developed and evaluated the suction capabilities of the novel versus the conventional video laryngoscope blade. To test this suction blade, a protocol evaluating its utility was conducted after IRB approval. The results of this work have been presented at the American Association of Anesthesiologists International meeting in October 2009 and have been submitted in manuscript form to the Journal of Clinical Anesthesia.

3: Determine and implement necessary design and manufacturing modifications for optimal device performance of the prototype video laryngoscope blade with an integrated suction channel.

- Design and manufacturing modifications were developed for optimal performance of the video laryngoscope blade.
- Follow-on funding has been submitted to transition the final prototype into a fielded FDA-approved device.

4: Deliver a final prototype pre-production indirect video laryngoscope blade with an integrated suction channel for clinical verification.
A final working prototype video laryngoscope blade with integrated suction channel was developed by Karl Storz Endoscopy Inc. and evaluated on a hemorrhagic airway simulator by the Center for Advanced Technology and Telemedicine.

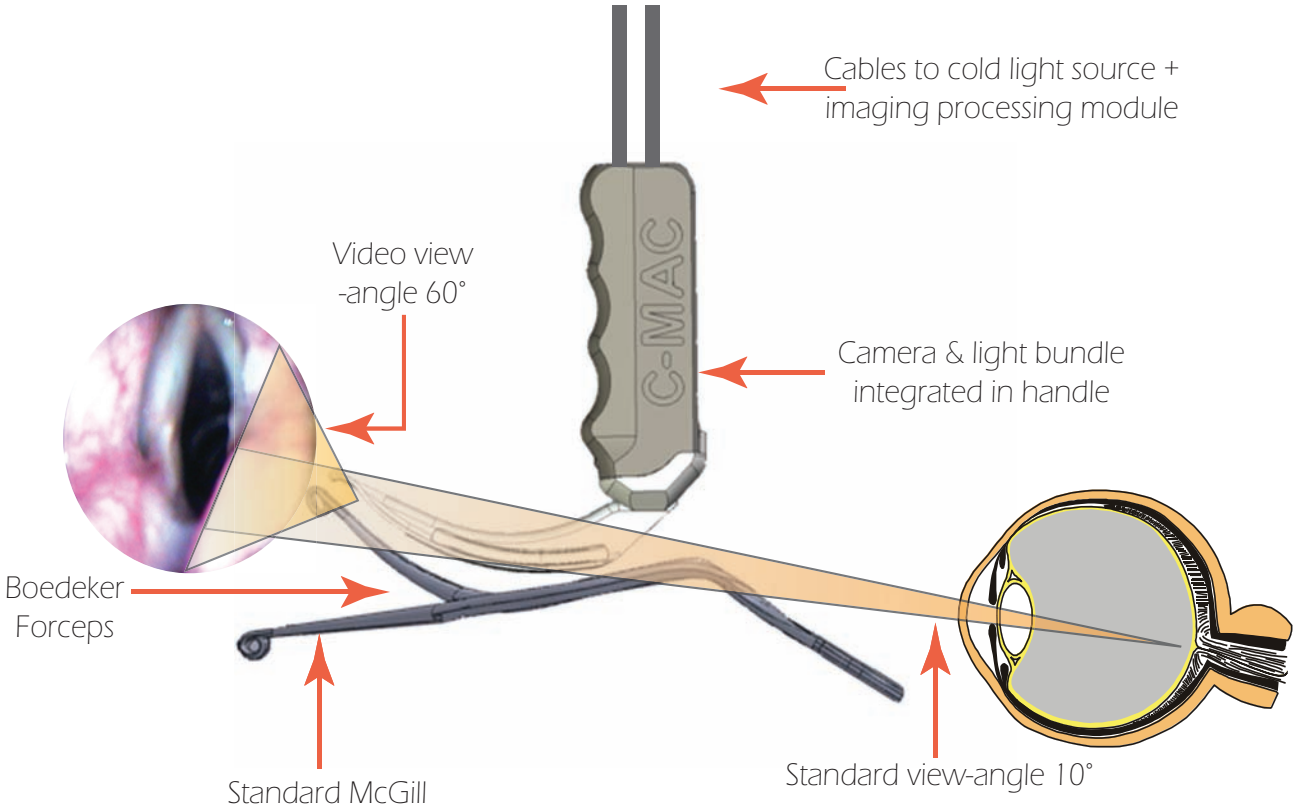
the field of view to accomplish manipulation of an endotracheal tube or removing foreign bodies is crucial when performing an intubation through the nose (necessary if the mouth is severely injured) with a video laryngoscope or removing a foreign body.

The Video Laryngoscope Blade was evaluated in a Simulated Airway Model with Secretions. The hemorrhagic airway creates difficulty in airway visualization, impeding attempts to successfully perform intubation. Challenges in development of a suction laryngoscope include insufficient suction rates and complicated methods of attaching catheters, making the device difficult to use. Video laryngoscopy requires optics free from distortion. This work compared a specially designed video laryngoscope blade with an integrated suction capability, and its comparison to, and support of, a standard suction system. The new system was comparable to and in many ways superieor to the older systems. The significant difference between each individual type of suction and the combination of the two indicate that using both during a procedure would increase the amount of blood and debris removed from a severely bleeding airway. The laryngoscope blade is present in almost every intubation, so integrating suction provides an additional avenue for removal of liquid from the airway while freeing the practitioner's hands for other tasks.

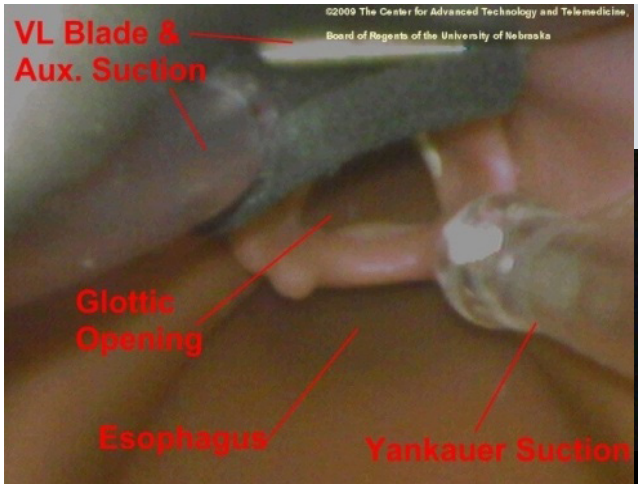
The results of this work were presented at the American Association of Anesthesiologists International meeting in October 2009 and submitted in manuscript form. Follow-on funding has been is in process to transition the final prototype into a fielded FDA approved device.

The Boedeker (Curved) Intubating Forceps for Removal of a Foreign Body have also been evaluated in a manikin. Foreign body aspiration is a common clinical problem, especially in children. The foreign body is commonly removed using McGill forceps and direct laryngoscopy (DL). While standard laryngoscopes provide a direct view along the line of the sight (10-degree field of view), with videolaryngoscopy (VL) a much wider (60-degree) field of view may be achieved. Conventional (straight shaft)

Using Intubation Forceps with a Video Laryngoscope



Comparison of field of view of direct and indirect laryngoscopy and the orientation of forceps tips with respect to field of view.



Left: Airway opening of a manikin with both types of suction installed. Center: Boedeker forceps and glottic opening. Right: The curve of the Boedeker forceps compared to that of a MacIntosh blade.

McGill forceps are designed to operate in direct line of sight. However, when using VL, the working end of this instrument does not pass into the laryngoscopist's field of view. The Boedeker Intubating Forceps was developed to allow the operator to reach into the full field of view offered by VL. In this testing, a curved forceps, bent in an arc similar to the MacIntosh blade, was shown to offer advantages for retrieval of foreign objects passed beyond the field of view by straight line of sight. This study demonstrated that the successful removal of foreign bodies using a forceps which is curved to match the shape of the MacIntosh laryngoscope blade is significantly more effective than using a forceps with a non-curved shaft.

These two instruments, the novel suction blade and the novel laryngeal retrieval forceps, have been licensed and production has begun by medical manufacturers. This is an example of new inventions being transitioned from concept through prototype to full licensed product supported only by TATRC's augmentation funding.

Video Laryngoscope Representative Publications

Boedeker, B. et al. Endotracheal Intubation comparing a Prototype Storz CMAC and a Glidescope Videolaryngoscope in a Medical Transport Helicopter – A Pilot Study. *Studies in Health Technol Informatics*. 2009; 142; 37-39.

Boedeker, B. et al. Endotracheal Intubation in a Medical Transport Helicopter –Comparing Direct Laryngoscopy with the Prototype Storz CMAC Videolaryngoscope in a Simulated Difficult Intubating Position. *Studies in Health Technol Informatics*. 2009; 142: 40-42.

Boedeker, B. et al. Airway Intubation in a Helicopter Cabin: Video vs. Direct Laryngoscopy in Manikins. *Avia Space Environ Med*. 2009; 80: 820-823.

Boedeker, B. et al. What's New above the Cords? Simulation Based Education for Supraglottic Airway Management. *J Mil Veterans' Health (Aus)*. 2009; 14: 10-11.

Boedeker, B. et al. Airway management: Shining a New Light. *J Mil Veterans' Health (Aus)*. 2009; 17: 8-9.

Pathogen Inactivation System

CaridianBCT, Inc.
Lakewood, CO

Securing the Safety of the World's Blood Supply

The last 20 years of scientific efforts have paved the way to secure a much safer global blood supply. Yet, pathogens such as viruses, parasites, and bacteria continue to emerge and re-emerge worldwide, increasing the demand for processes to mitigate the risks of blood transfusions. Blood Bank Centers face an increasing demand on testing processes as they react to these new and emerging pathogens by developing appropriate testing for donated blood. In addition, many regions around the world still do not have the resources and technology to test for many of the potentially lethal or debilitating pathogens that may be present in the life-saving gift of blood.

To address this challenge, CaridianBCT has developed a way to reduce disease-causing agents and inactivate white blood cells that can contaminate blood products intended for transfusion. CaridianBCT Biotechnologies' Mirasol® Pathogen Reduction Technology (PRT) System, using ultraviolet light and riboflavin, an essential nutrient also known as vitamin B2, has seen extensive research, development and testing since 1999.

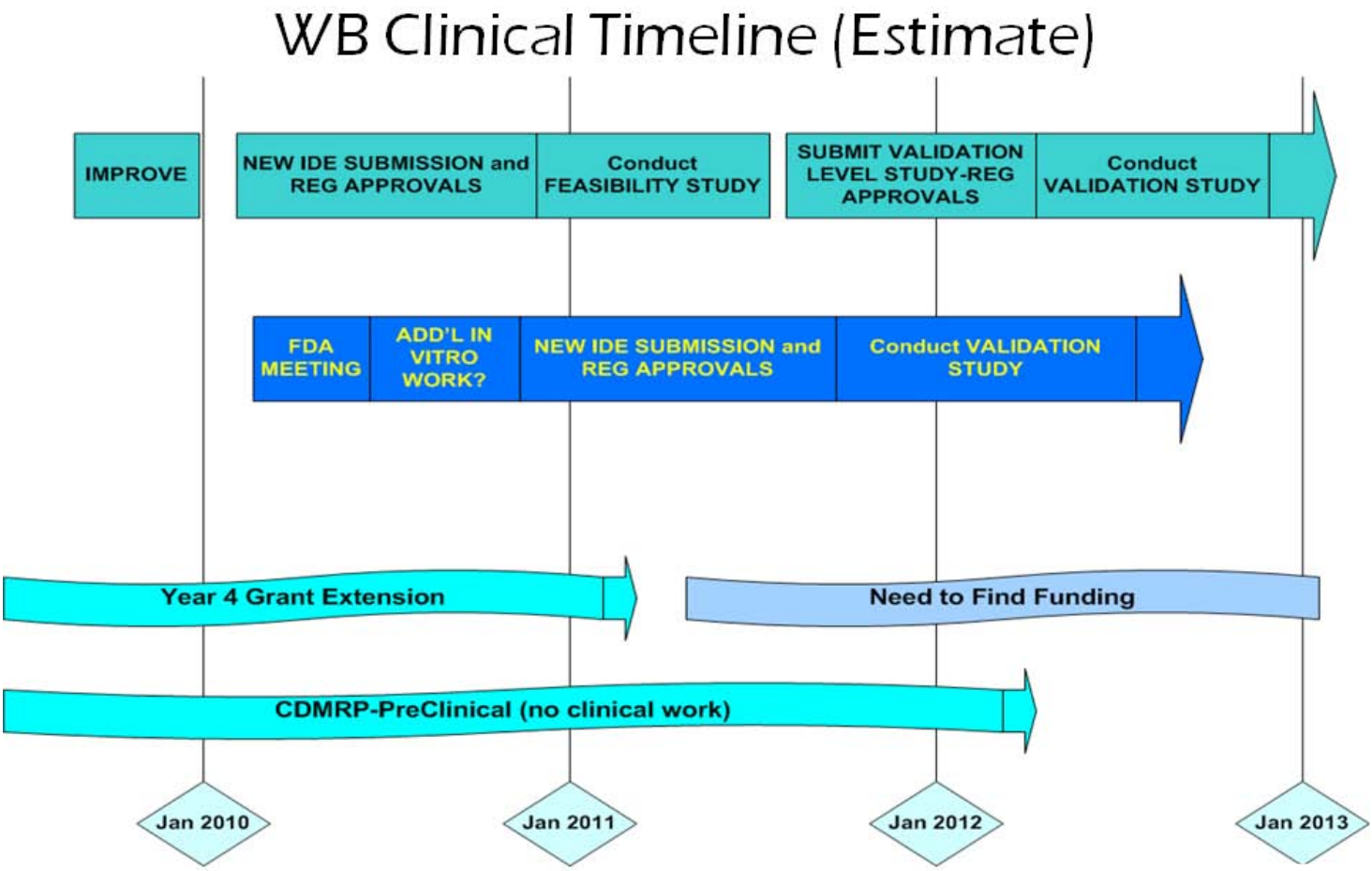
As the US deploys troops around the world, securing a safe and available blood supply is vital for the brave men and women already facing the dangers posed by the enemy and hostile foreign environments. Lifesaving transfusions are often performed near the battlefield under extreme conditions. As donor screening and infectious disease testing is difficult in these surroundings—and in many cases, impossible—a wounded Warfighter's "blood bank" may be the comrades fighting alongside. In these trauma situations, time is of the essence. The sooner safe blood can be provided and the safer that blood is, the better the chances of survival.

"Our process is proactive and universal; we don't have to know exactly what pathogens are in the blood in order to inactivate them. In one treatment, we reduce the risks arising from any bacteria, virus, parasite, and donor white cell contamination of donated blood products."

Dr. Raymond Goodrich, CaridianBCT

Then: World War II Battle of Tarawa first aid station's blood bank.

Now: Mirasol™ Pathogen Reduction Technology (inset) procedure for allows for safer blood to be provided on the battlefield.



WB – Whole Blood
FDA – Food and Drug Administration
IDE – Investigational Device Exemption
Reg – Regulatory Approval

Supporting these men and women in the line of duty, the DoD, USAMRMC, and specifically TATRC, are working with CaridianBCT Biotechnologies to ensure the safety of blood products used in transfusions for military personnel injured in combat. Research has shown that for trauma cases in the field—where the use of fresh whole blood is often put into practice—transfusion of whole blood has a significant positive impact on patient outcomes, including survival.

TATRC is assisting CaridianBCT Biotechnologies' development of the Mirasol PRT system as a transportable system to treat whole blood, thereby reducing the risks associated with blood-borne pathogens and donor white cells. As a lightweight, portable device, the Mirasol PRT system has the potential to introduce safer blood with fewer complications, providing a new way for military and civilian surgeons and transfusion medicine specialists to aid patients with life-threatening blood loss.

Pathogen Inactivation Representative Publications

Goodrich RP, Murthy KK, Doane SK, Fitpatrick CH, Morrow LS, Arndt PA, Reddy HL, Buytaert-Hoefen KA, and Garratty G. Evaluation of potential immune response and in vivo survival of riboflavin-ultraviolet light-treated red blood cells in baboons. *Transfusion*. 2009;49:64-74.

Reddy HL, Dayan AD, Cavagnaro J, Gad S, Li J, and Goodrich RP. Toxicity Testing of a Novel Riboflavin-Based Technology for Pathogen Reduction and White Blood Cell Inactivation. *Transfusion Medicine Reviews*. 2008; 22: 133-153.

Goodrich, RP, Doane, SK, and Reddy, HL. Design and Development of a Method for the Reduction of Infectious Pathogen Load and Inactivation of White Blood Cells in Whole Blood Products. *J Biologicals*. 2009; 10.016.

Rugged Mobile Logistics System (RMLS)

VerdaSee Solutions, Inc.
West Langhorne, PA

The Rugged Mobile Logistics System (RMLS) consists of a number of intelligent, rugged, portable hardware items, integrated by VerdaSee to provide critical information at the local, regional and global levels. A top-level block diagram of the regional configuration of the system is shown below.

The hardware components are a mixture of Commercial off-the-shelf (COTS) and COTS products that have been modified and enhanced by VerdaSee to meet the project needs; and some of the hardware/software components are custom-designed by VerdaSee specifically for the RMLS. RMLS nodes can support large and small, fixed and mobile, warehouses, depots and terminals.

RMLS is an economical, innovative and unique combination of COTS hardware and software elements. An example of the uniqueness is the ability to track supplies carried within containers, down to a single item, such as a pill bottle. The GPS-enabled system provides near real time data and information with graphics displays linked to standard enterprise systems to provide local, regional and global visibility of assets at a granularity and in a presentation model needed by the specific users accessing the system.

The VerdaSee RMLS is also unique in that it is modularly designed for continuous improvement and scalability. As VerdaSee's hardware and software components and subsystems improve over time, they can be seamlessly incorporated into in-place systems. In this way, the outdated versions of the components/subsystems can be replaced or added to expand the RMLS capabilities. As such, the deployed RMLS systems can evolve and expand without having to discard the initially deployed

Rapidly Deployable, RMLS for Operational Environments.

system, which minimizes the issue of obsolescence. An example of this is the VerdaSee Navigator Middleware™ and the Enterprise Logistics Management System™ that reside on the RMLS server. The middleware allows for integration to multiple inputs and outputs without disturbing the logistics management system. The same is true for the hardware components, such as the Steerable Phased Array Antenna (SPAA). The SPAA will track passive RFID tags that comply with the Gen 2 global standard, regardless of the manufacturer of the tag, or the form factor. The SPAA is only one example of the State of the Art components that are being presented in this system. RMLS will allow for a migration path to the future as other components evolve into even greater capability.

Though the design focus is for austere deployments, government and commercial, the RMLS provides the same advantages for permanent installations. Low power, lightweight, easy to operate, modular, scalable; these are all qualities that are useful, if not necessary in permanent installations.

The RMLS is based on a technology platform rather than a single specific product. Therefore, in a sense, it provides many possible applications and products within the system. The separate applications, or components, can be delivered individually; multiple components can be integrated to become a useful subsystem; or the entire system can be delivered as an integrated enterprise wide solution. The delivered solution is based on best of class components available commercially, and enhanced to achieve the desired functionality and performance. By focusing on the platform, the individual components can be upgraded independently without disturbing the other components in the system.

This design protects the end-user community from the issue of obsolescence that otherwise burdens the traditional approach to logistics management that is software or product-driven. For example: if an Intermec handheld scanner is currently being used, the end-user can continue to deploy it because the Intermec data output can be integrated through VerdaSee's Mobile Logistics System™ middleware; competitive designs may mandate the conversion to a new hardware standard, thus destroying the value of the prior investment. Correspondingly, if an end-user chooses to deploy a new scanner (i.e., from another manufacturer), the new scanner can be quickly integrated through the middleware, allowing for a migration path to updated components, while protecting current investments in tracking technology. Another alternative provided by the VerdaSee system is to employ the multi-frequency scanner being provided in the RMLS while retaining other components already in place until it is practical to replace them.

VerdaSee's focus is to provide the DoD with a system that delivers the full range of requested capabilities with uncompromised quality and consistency. It recognizes the need to deliver systems that are easy to use and quick to deploy in ever-changing and often austere environments. It also recognizes the need to provide solutions that seamlessly integrate with existing technologies, preserving the DOD's current investment, and to provide a cost-effective migration path with respect to future technological innovations.

Frequent demonstrations of the Rugged Mobile Logistics System have been provided to DoD agencies, First Response agencies, Humanitarian Relief organizations, and various commercial Logistics companies during the current Phase II development period.

Rugged Mobile Logistics System Publication

Y. Zhang, K. Yemelyanov, X. Li, and M. G. Amin, "Effect of metallic objects and liquid supplies on RFID links, " IEEE AP-S International Symposium on Antennas and Propagation and 2009 USNC/URSI National Radio Science Meeting, Charleston, SC, June 2009.

Significant Meetings

The convening function at TATRC is a crucial tool for advancing medical science and technology within the DoD. Key meetings this year helped to raise visibility of important initiatives. The meetings included the Amercian Telemedicine Association (ATA) TATRC Day's meeting on the "Personal Health Record," (p. 154); the TATRC Advanced Medical Technology Exposition (p. 157), which increased the visibility of mature technology areas; the TATRC/ University of California (UC) Bioengineering Grand Challenge, which inspired new researchers to work on military medical problems (p. 156); and two meetings that promoted innovation and facilitated the earliest possible information exchange within fast moving fields of research—The Virtual Human Workshop (p. 155) and the Military Refractive Surgery Conference (p. 157).

Product line reviews (PLRs) occurred at least monthly—there were 17 major PLRs in 2009 each customized to a collection of projects within a topic area—with review panels of 15-25 diverse experts including military customers and requirements drivers, contracting specialists, industry/tech transfer experts, and other federal agencies including including the NIH, VA, and FDA, along with many top subject matter experts. PRLs are the "in process" reviews of funded projects within a program or topic area. These are different than another TATRC tool, the Program Review Board (PRB), that meets weekly to make funding recommendations on pre-proposals and full proposals. We have highlighted three of this year's PLRs in this section: Complementary and Alternative Medicine Treatments of PTSD and TBI, Blood Products and Safety, and Disaster Response (pp 161-167).

American Telemedicine Association (ATA), TATRC Day

April 25, 2009
Las Vegas, Nevada

In conjunction with the 2009 American Telemedicine Association annual meeting, TATRC hosted an intense 11-hour symposium organized by Dr. Jean-Louis Belard and LCDR Steve Steffensen. This was an in-process review of military informatics research efforts and their linkage to concepts for the military health information systems; attendees included key decision makers in the Military Health System (MHS).

Keynote speakers, Mr. Charles Campbell (CIO for the MHS) and LTC Hon Pak (CMIO for the US Army), challenged the group to work toward common themes identified for the MHS such as a stable longitudinal health record and interoperability, as well as fundamental changes in business practices that must occur with the electronic health record. Dr. Charles Peterson, Chief Scientist for TATRC, exhorted the group to creative solutions, asking the central question: "How can we delight our customers?" This referred to the problems of speed, reliability, and useability of AHLTA currently discouraging users. LCDR Steffensen provided a comprehensive overview of TATRC's congressional special interest and other projects, illustrating key gaps in the current architecture with multiple examples of how projects have been directed to address those needs, and he provided a preview of next year's health IT with the interconnectivity of the VLER.

The remaining dozen speakers addressed topics in three areas – megatrends in personalized health, the impact of mobile technologies, and the personal health record. Megatrends included examples of therapeutic drug policy changes that have occurred in the past year as a result of the analysis of EHR health outcomes data in the pharmacovigilance program led by COL Trinka Coster; Dr. Jack Smith (Dean, School of Health Information Sciences, UTHSC-Houston) wrapped up the session with a view into the future of cognitive support in personalized health. TATRC's ever expanding involvement in mobile technologies was well represented and also endorsed in a session highlighting how personal communications devices are already improving medical care for Warfighters. The great challenges of producing actionable knowledge for individuals and health care providers in a personal health record were addressed with examples of current approaches in automated physiological data acquisition to assess changes in health status, and other topics of semantic web, computational tools, and biostatistical approaches, where true interdisciplinary efforts are needed to solve these problems. Mr. Rick Cnossen (Continua Health Alliance) closed the meeting with a glimpse of the future in personal telehealth based on technologies that are largely available today.

ATA TATRC Day Themes

2007	Hospital of the Future
2008	Personal Health Monitoring
2009	**Personal/Electronic Health Record**
2010	m-Health
2011 (forecast)	International e-Health Partnerships

Virtual Humans Workshop

April 29 – 30, 2009
Marina del Rey, California

The mission of the Virtual Human Workshop was to create a synthetic experience such that the participants will react as if the situation is real. Key elements included:

- Immersion
- Virtual Humans
- Graphics
- Games & Simulation
- Narrative and Storytelling

The meeting, held in April 2009, was purposed to discuss virtual humans as the University of Southern California ICT, and to come up with 10 important areas for futural development in virtual psychoanalysis and virtual human technology.

To create a virtual psychological analysis, the group defined several parameters—the data collection must be automatic with limited access to the results due to ethical issues; the system must be able to capture behavioral data such as patient interaction, non-verbal communication, and facial expressions; and the system must perform some sort of cognitive analysis on the verbal queues that are portrayed by the patient. It needs to be able to understand natural spoken language and speak naturally so that the patients don't feel as though they are speaking to a robot. These forms of analysis could be used to help Warfighters deal with major depression, substance abuse, PTSD, or family conflicts.

The group then looked at how to get from the current technology to the system mentioned above. This started with an analysis of the current state of technology. There are several virtual psychoanalysis programs that have been developed at ICT; none of them completely meet the needs initially set forth by the group, but they are a step in the right direction. There are funded projects that display natural language speaking, and the database of colloquialisms is constantly expanding so that the trainer can understand anything a patient might say.

The ICT has also developed virtual patients which portray non-verbal as well as verbal queues so that therapists in training can understand how a patient might act. The next step, now that these queues are known, would be to translate everything into recognition software.

There are several new efforts being set forth to ensure progress in this field. A lifestyle coach is being built. This will be designed to test cognitive and physical readiness, and point a patient in the right direction of a therapist who might be able to help. A virtual reality psychological test is being created to asses a patient's condition using neuropsychology instead of cognitive queues. The newest effort in this field is the creation of a SimCoach (pp. 143-144) which is focused on people who tend not to seek out help. This coach would provide help for both families and Warfighters.

A virtual human provides a sense of personal interaction between the patient and technology.

Bioengineering Symposium

June 19 – 21, 2009
Merced, California

University of California System-wide Bioengineering Symposium

The University of California (UC) System-wide Bioengineering Symposium had its 10th annual meeting at the newest school in the UC system, UC Merced. The main purpose of the symposium is to provide students with the chance to learn about other research efforts conducted throughout the region and to develop their professional skills. This meeting consisted of graduate students, professors, and world experts. TATRC's involvement in the UC Bioengineering Symposium is rooted on two functions: 1) help support the annual meetings; and 2) seize the opportunity to raise awareness about military medical needs.

UC Merced was the meeting place for the University of California Bioengineering Symposium.

The meeting mainly consisted of several track sessions, highlighted by keynote presentations that helped to set the stage for the day's proceedings. These keynote presentations help to provide insight into new research, and the need for early consideration of a commercialization strategy. The keynote presentations also provided TATRC the opportunity to raise awareness on the medical needs of the military.

In general, the track sessions consisted of student research presentations focused on specific topics within biomedical engineering (Biomaterials, Nanotechnologys, Tissue Engineering, etc.). These sessions allowed students to learn about research effort conducted in other labs, and they also provided the students an opportunity to present their work in front of their peers, professors, and other experts in the room. This allowed the presenters, and attendants, the chance to receive feedback that could help shape their future research efforts. Presenting in these sessions also helped the student refine their presentation skills, as these highly knowledgeable audiences demanded that the presenters have well prepared slides and answers to a large array of focused questions.

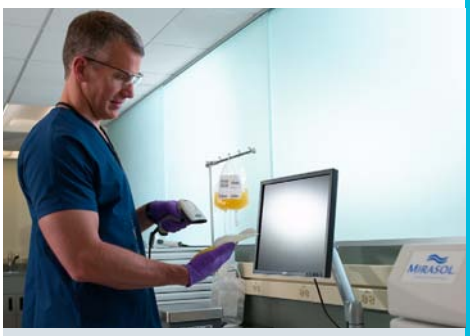
In the keynote presentation on military medical needs, Dr. Charles Peterson (TATRC's Chief Scientist) enlightened the symposium attendees on: the range of medical research topics the military is interested in, how the military is involved in these topics, and what unique limitations and requirements need to be considered in developing medical technologies for the military. Dr. Peterson's presentation also announced TATRC's Grand Challenge to the graduate student community. The Grand Challenge engages the students to submit military relevant research proposals. At the following symposium, the top five submissions would be announced and they would receive financial awards to conduct the proposed efforts. This challenge's purpose is to implore the next generation of researchers to be aware of, and consider, the specific needs of the military for medical technologies.

Through participation in the annual symposium, TATRC's ultimate goal is to help future researchers understand that there are additional genres of medical research to be considered within the military. In addition to this, TATRC hopes to help the students develop their professional skills by providing more opportunities: to submit research proposals, and to give presentations in front of knowledgeable audiences. Through these efforts, TATRC hopes to help develop the future researchers that will be working on military relevant medical technologies.

Advanced Medical Technology Exposition

June 17 – 18, 2009
Fort Detrick, Maryland

The USAMRMC/TATRC "Advanced Medical Technology Exposition" was held in June 2009 in the Oasis concept deployable hospital at Fort Detrick. The event showcased a variety of technologies leveraging various funding sources (Congressional Special Interest and SBIR/STTR) in the areas of simulation, robotics, informatics, medical logistics, deployable telemedicine and technologies for the combat support hospitals. Demonstrations were scheduled throughout the two-day event.



A new portable system uses Mirasol™ (riboflavin) and UV light to inactivate disease-causing organisms in donated whole blood.

Robotic combat casualty assessment and extraction prototypes by Applied Perception Inc. (left) and American GNC (right).

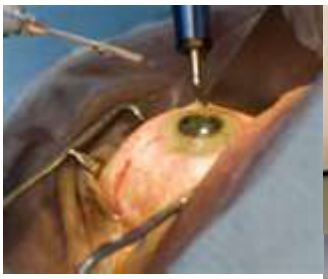
Forty-nine organizations were on site to demonstrate their advanced medical technologies. The event provided an invaluable opportunity for networking and learning about upcoming future technologies. The technology exposition increased awareness, and facilitated communication and collaborations among exhibitors and attendees. This exhibition allowed TATRC to build community relations and showcase its capabilities to the USAMRMC command, the city of Frederick and the general public.

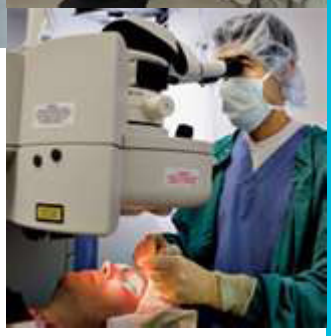
TATRC representatives were available to discuss initiatives with Advanced Medical Technology Exposition attendees.

International Military Refractive Surgery Conference

January 5 – 7, 2009
San Antonio, Texas

Valuable information regarding surgical techniques, complications, patient safety, surgical eligibility, medical policy, coding, and budgets was shared among the three services in attendance. In addition to United States Military refractive surgeons, there were representatives from, Canada, France, Great Britain, Israel, Japan, Turkey, Germany and Singapore.





The objectives were to discuss the latest scientific research being done at military refractive surgery centers; discuss current medical issues in refractive surgery such as advanced techniques for corneal refractive surgery, indications for surgery, and prevention and treatment of complications; and describe current policies for refractive surgery in the US Military and international militaries. This meeting was supported by TATRC.

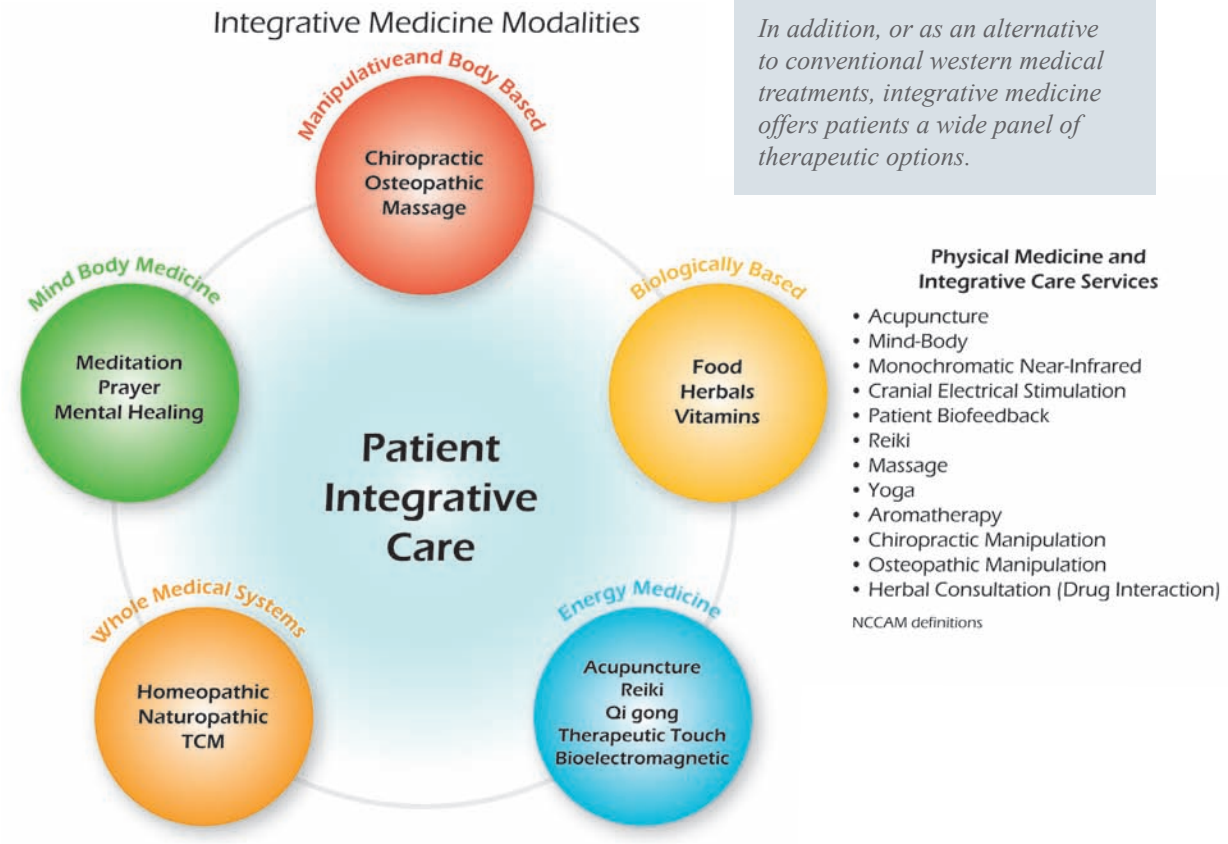
Strategic Planning Meetings

October 22, 2009
Frederick, Maryland

Under the leadership of Dr Stephen Schimpff, former professor of internal medicine, CEO of of the University of Maryland Medical Center, and author of "The Future of Medicine: Megatrends in Healthcare," TATRC has setup a series of Strategic Planning meetings to discuss the role that TATRC should have in critical domains. In October 2009, TATRC sponsered a workshop on Pain & Integrative Health (IH) Strategic Planning. The morning was devoted to presentations by experts including Dr. Robert Bonakdar, Director of the Pain Clinic, Scripps Institute; COL Trip Buckenmayer, Director of Regional Anesthesia and Pain Management, WRAMC; Dr. Herbert Benson, founder and Director Emeritus of the Boston Mind-Body Institute; Dr. Margaret Chesney, Deputy Director of the Integrative Medicine Center, University of Maryland, and now Director of the University of San Francisco Integrative Medicine Center; and COL Richard Petri, Director of the DoD first Integrative Medicine Center, Ft. Bliss, TX. In the afternoon, attendees were split into three groups. Each group participated in round tables focusing respectively on chronic pain, acute pain and integrative health. Attendees shared their views on what needs to be done to make IH interventions more accepted by the medical establishment and the military leadership and more easily understood by and available to patients. The meeting concluded with the definition of a set of goals and objectives for TATRC.

The following recommendations were made:

- obtain in two weeks an inventory of DoD facilities offering IH interventions.
- spread the concept that IH is the future for treating pain through articles outlining the need for IH and multi disciplinary pain centers to be published in professional journals.
- include IH interventions in personal EHRs.
- develop SBIR along with allocating more gap funding to study IH interventions, including new tools, treatment protocols, especially to serve our deployed forces.
- develop mechanisms to nurture patient empowerment through education, offer patients access to relevant data so they can benefit from enhanced personalized medicine.



In addition, or as an alternative to conventional western medical treatments, integrative medicine offers patients a wide panel of therapeutic options.

Product Line Reviews (PLR) and Workshops

Morningside Inn, Frederick Maryland

Overview and Schedule

The purpose of the Product Line Review (PLR) is to provide a portfolio level assessment of each TATRC managed project by a panel of subject matter experts. The PLRs are conducted once or twice a month and each portfolio is provided a review every 12–18 months. A facilitator is assigned to the PLR to enable effectiveness, collaboration and synergy among the attendees.

The reviews are held at The Morningside Inn in Frederick, MD, unless the PLR is scheduled to coincide with a major scientific review meeting which is representative of the portfolio and the projects therein. Occasionally, the portfolio manager may decide to conduct a review of projects within a geographical location or organization in that topic area.

The PLR provides the TATRC Director and Senior Staff project updates in the areas of funding, timelines/progress, protocol approvals and any other pertinent issues which may affect the course of the research effort. The PLR also:

- Provides the Principal Investigator with immediate panel feedback;
- Provides agencies outside of TATRC the opportunity to shape the research effort to satisfy specific operational needs;
- Identifies candidates for tech transfer/ commercialization;
- Provides an opportunity to identify research gaps which could be addressed through the submission of a SBIR/STTR topic; and
- Provides the Contracting Office Representive/ Project Officer (PO) an opportunity for face-to-face interaction.

Panel members listening to a presentation during the Infectious Disease PLR in July 2009.

PLRs provide opportunities for networking between investigators and other attendees, as well as opportunities for collaborations that can result in improved products/outcomes.

The PLR panel is chaired by the respective portfolio manager and coordinating partner from one of the RADs (Infectious Disease, CCCRP, MOMRP, CRMRP). The panel consists of 20 – 30 subject matter experts representing academia, industry, DoD and other Federal agencies. The panel provides feedback to investigators as well as the management team on the areas of scientific/technical merit and progress; identification of redundancies; cost/schedule/performance; technology transfer potential; areas for improvement; and opportunities for collaboration/leverage to promote other research projects

Projects presented at the PLR can be at different stages of completion including:

Beginning:

- The review provides an opportunity to guide and shape research direction

Ongoing:

- During the course of the review, feedback may indicate the need to do a course correction to bring the research more in line with portfolio/ core gaps or written requirements

Complete or nearly complete:

- The deliverables from the completed research can be considered for transition strategies, i.e., advanced development , commercialization or fielding.
- Components of larger projects (such as congressionally-funded centers or other efforts with a broad scope.

During FY09, TATRC managed over 800 projects within its various portfolios. The PLR is an effective tool which provides the opportunity to shape and manage these investments through the identification of research gaps and SBIR topics; leveraging partnerships, networking opportunities, and collaborations; and the provision of support to high-risk, far forward, cutting-edge research which enhances medical care on and off the battlefield.

In addition to PLRs tailored to various review and strategic planning goals, TATRC used site reviews involving visiting external scientists for peer review of important projects.

These included projects at various stages of completion including important long standup investments such as the brain mapping effort at University of Oregon on "Brain Biology and Machine," the Comprehensive National Neuroscience Program (CNNP) efforts, and the Center of Excellence for Remote and Medically Under-Served Areas (CERMUSA) effort at Saint Francis University (Loretto, PA), June 2009. The reviews provided investigators and TATRC with expert advice on strategic planning for the next steps; long range directions, and technology transfer.

AIBS review panels were also used to help several investigators substantially reshape their experimental designs for difficult studies that fill critical military medical gaps.

2009 TATRC Product Line Reviews

Medical Modeling and Simulation (Long Beach, CA)	22 January 2009
Complimentary and Alternative Medicine in Support of DCoE	3 February 2009
Neurotrauma (West Coast, LAX Marriot)	10-11 February 2009
Healthcare of the Future (Medical IM/IT)	24 February 2009
Large Scale Disaster Response	21 April 2009
Behavioral Health/PTSD/Tele-mental Health	5 May 2009
Biomonitoring Technologies	19 May 2009
Neurotrauma	9 June 2009
Blood and Blood Safety	23 June 2009
Rehabilitative Medicine/Military Amputee Research Program	14 July 2009
Infectious Disease (chaired by JTCG2)	28 July 2009
Regenerative Medicine (co-chaired with JTCG6 & JTCG8)	18 August 2009
Imaging & Medical Logistics	1 September 2009
Neurotrauma - Spinal Cord	29 September 2009
Biomaterials and Nanomedicine	15 October 2009
Resilience and Reintegration (collaborative with service proponents)	27 October 2009
Proteomics and Genomics	5 November 2009
Ocular Health	17 November 2009

Complimentary & Alternative Medicine in Support of DCoE

February 3, 2009

As part of a larger program of system wellness and integrated health TATRC, in collaboration with the DCoE is investigating non-traditional treatment of psychological health for our Warfighters. These projects encompass non-traditional medical approaches such as mindfulness, self compassion meditation, virtual reality, acupuncture, yoga, use of service animals as well as affordable readily available technologies such as cell phones.

In February 2009, the principal investigators of these projects presented to experts representing all branches of the DoD. The presenters received constructive comments from the group on how to better tailor their efforts to DoD gaps and requirements, and increased interaction between each other allowing them to synchronize their efforts. This program will scientifically evaluate and validate the effectiveness of techniques in the treatment of combat related PTSD, TBI and other psychological illnesses and transition useful prophylactic and therapeutic approaches into practice.

One of these projects is investigating the use of psychiatric service dogs in the treatment of Veterans with PTSD. In this project the authors will establish a legitimate evidence base through rigorous clinical research; this study proposes to provide 10 carefully screened rescue dogs to 10 Soldiers with PTSD who reside at WRAMC. The new human-canine partnerships will be round-the-clock. The 10 Soldiers with dogs will be taught how to train their dog in three domains: basic obedience, public access skills, and disability-related assistance. The training will take place over six months under professional guidance, and each dog will graduate from the training program as a full-fledged Service Dog with public access privileges, similar to a Guide Dog.

COMPLIMENTARY & ALTERNATIVE MEDICINE FAST FACTS

Projects funded: 10
Total funding: $5 Million for FY09
Duration of projects: 18 months
These projects encompass non-traditional medical approaches including:
- **Mindfulness**
- **Self compassion meditation**
- **Virtual reality acupuncture**
- **Yoga**
- **Use of service animals**
- **Cell phones**

Senator Ensign requested a briefing on the TATRC-funded project on the use of psychiatric service dogs.

Another set of 10 Soldiers with PTSD will be utilized as a comparison group; they will not receive a dog. Both groups will undergo the same usual treatment protocol for Soldiers with PTSD at WRAMC. Both groups' mental health will be studied by research clinicians for 12 months and data collected from both groups will be compared.

A second project will evaluate acceptability of and compliance with a yoga treatment for PTSD in military Veterans and will also evaluate treatment efficacy and associated PTSD characteristics and symptoms. The rationale for this study includes the concepts that:

- yoga may be an effective intervention for military Veterans with PTSD;
- additional effective and adaptable

behaviorally-based treatments for PTSD need to be developed to expand the repertoire of effective treatments available and because current treatments show a number of limitations; and

- military Veterans are already applying these techniques as treatments for PTSD in the absence of research on efficacy.

This study will add to research into the mechanisms underlying PTSD and its treatment. The proposed 18-month feasibility/efficacy trial will recruit military Veterans with PTSD meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria and subject them to a 10-week yoga intervention.

LTC Erica Clarkson, DPT performing acupuncture for sinus headache on Soldier at a women's health seminar in Baghdad, Iraq.

The intervention will include a full spectrum of yoga practices including physical postures and exercises, yogic breathing techniques, meditation, cultivation of mind/body awareness, deep relaxation, and training in the psychology and philosophy of yoga. Subjects will undergo biweekly 90-minute group yoga classes and a prescribed 15-minute daily practice at home throughout the 10-week intervention. Outcome measures will be acquired at baseline, at post-treatment and at a three-month long-term follow up in both groups. PTSD severity will be evaluated with the Clinician-Administered PTSD Scale (CAPS). Psychophysiological arousal levels will be evaluated with 24-hour urine samples for assay of catecholamines and with electrocardiographic recordings with heart rate variability analysis to evaluate sympathovagal balance. Subjects will also complete self-report questionnaires for depression, anxiety, sleep, quality of life and acceptability of the treatment. Treatment tolerability and compliance will be evaluated with a daily log and interviews.

Another project from this program will determine whether the participation of Veterans in mind-body skills group will significantly decrease symptoms of PTSD; decrease feelings of anger; improve quality of sleep; decrease symptoms of depression and anxiety; increase post-traumatic growth; and increase quality of life.

The study design will be a randomized controlled study. One hundred sixty Veterans meeting the criteria for inclusion will be randomized to participate in either an intervention group (consisting of a series of mind-body skills groups) or a control group (consisting of treatment as usual).

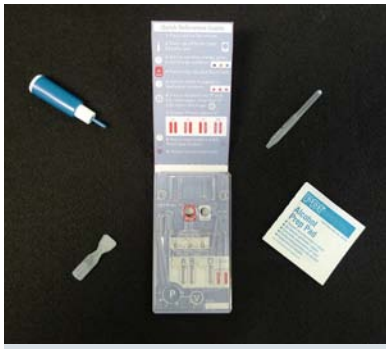
The mind-body skills groups will each have eight to ten participants and include the teaching and practice of meditation, guided imagery, and breathing techniques; self-expression through words, drawings and movement; autogenic training and biofeedback; and genograms. The groups will be held on alternate weekends over a three-month period with additional groups one- and three-months later. Pre- and post-questionnaires to measure each of the outcomes in the specific aims will be administered. The questionnaires will be administered again at six-month follow-up.

The review increased coordination between the individual projects in this program, helped to focus the group on the military medical needs to be addressed, and helped the program managers prepare for follow on studies and other transitions.

Blood Products and Safety

June 23, 2009

The Blood Products and Safety Portfolio presented its first official PLR in June 2009. The forum proved to be an outstanding venue for the peer review and future guidance of a select group of medical research projects with a primary focus on blood products and safety, biologics, drug and medical devices. The success of the initial PLR represents the contributions of the following TATRC staff: Wilbur Malloy-Portfolio Manager and Project Officers: Rebecca Duve, Manja Lenkin, Heather White, Samuel Vazquez, Dan Sarvaideo and Angela Sargent. The PLR included an internationally renowned review panel, which represented organizations from academia, business, and the federal government. Federal panel members included representation from the DoD (Human Research Protections Office, the USAISR, the AMEDD Center and School, USAMRMC, WRAIR, and the FDA Center for Biologics Evaluation and Research, Office of Blood Research and Review.



The Micronics ABO/RL blood-typing kit will indicate blood type and Rh factor in less than 30 seconds. The card is the size of a credit card.

The approach of the Portfolio is to collaborate with all aspects of science and engineering institutions (academic, government-military, civilian), to enable technology transfer in support of blood products, and safe clinical practices and outcomes.

The PLR encompassed 11 projects ranging from a microfluidic credit-card sized device to determine blood types, pathogen inactivation/reduction, organ and tissue preservation, sprayable liquid wound dressing, active thermal resuscitation, nano-therapeutics, oxygen diffusion dressings, and biomarkers and tissue engineering. Several of these projects are summarized below.

New Rapid Blood Typing Test

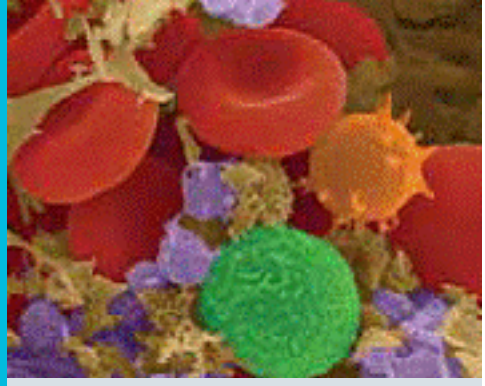
A new technology that provides a rapid, portable, cost-efficient way to determine the blood type of potential donors is now available to make blood collection safer for Warfighters in the field. Blood products from military collection centers do not always reach local areas of high demand because combat surgical units have limited blood storage capacity. Currently, medical personnel may have to wait hours or days to qualify a blood donor for responding to emergency blood supply requirements.

The new Micronics ABO/Rh Card is a disposable, credit card-sized device that can accurately determine the ABO blood type and Rh factor from a single drop of blood in less than 30 seconds. It is the first device that does not require refrigeration or supporting equipment and is packaged in a closed system to protect the blood sample and reagents from environmental contamination.

TATRC has been collaborating with Micronics, Inc.'s Dr. Diane Wierzbicki to help her team advance the card from research development to clinical validation. The ABO/Rh card is projected to be commercially available in 2010.

"The ABO/Rh Card will make it possible to recruit those with specific blood types for which there is the greatest need in an emergency. The card also provides another layer of information by enabling personnel in the field to quickly ascertain a Soldier's blood type and to confirm that it matches that shown on the dog tag."

Diane Wierzbicki, Ph.D.
Micronics, Inc.



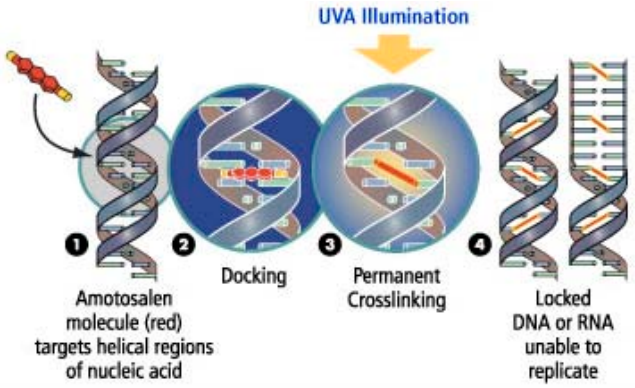
Red Cells have 29 blood group systems with more than 200 serological identifiable antigens. Genomic typing will increase that number by an unknown factor.

Genomic Typing of Red Blood Cells

Occasionally transfusion reactions occur even when compatibility testing with the current systems indicates that the cross-match is compatible. Furthermore, these tests are difficult to perform in emergency situations. Genomic testing of Human Erythrocyte Antigen (HEA) can lead to the development of high throughput screening systems to determine red cell donor-recipient compatibility within minutes. The researchers at the Puget Sound Blood Center are looking for frame shift mutations, stop codons, deletions or additions that could impair gene expression in sites previously not covered. Puget Sound Blood Center is advancing our knowledge of the 29 known blood group systems, which encompasses over 200 antigens located on the red cell surface with the development of micro-array typing and PCR–Restriction Fragment Length Polymorphism (PCR-RFLP) technology. This research will also establish genomic and phenotypic frequencies for several ethic populations that have not been studied before and are underrepresented with reference to knowledge about their red cell antigens.

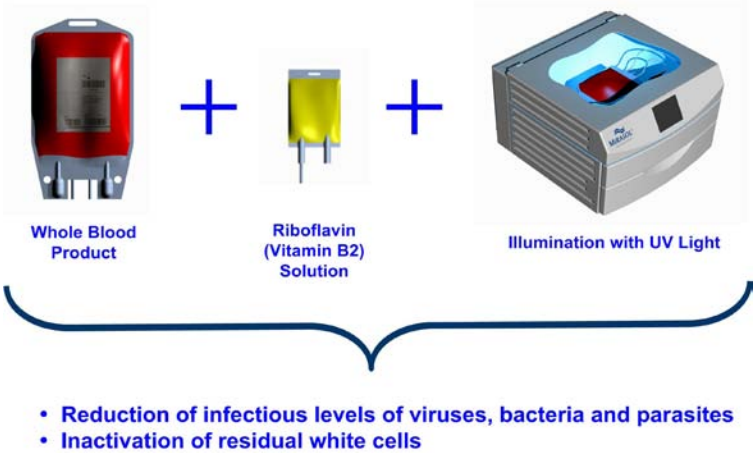
Pathogen Inactivation for Human Transfusion

Researchers at Cerus Corporation are developing technology to inactive a broad spectrum of pathogens and leukocytes in platelets, plasma and red blood cells. This technology will minimize a Soldier's risk of disease-causing pathogens as a complication of blood transfusion. Cerus and their Intercept™ Blood System utilize Amotosalem HCl and long wavelength ultaviolet light to penetrate cellular and nuclear membranes to inactivate leukocytes and pathogens rendering them unable to cause disease, while retaining the function of the plasma and platelets. The Intercept™ System for platelets and plasma is currently approved and available in Europe. With TATRC support, the red cell system met the development criteria to advance the project to a Phase 1 clinical trial in the United States.



The reproduction of pathogens can be blocked by cross-linking DNA and RNA.

Because screened whole-blood is typically not available for immediate combat casualty situations, and currently limited tests are available for new pathogenic organisms to which donors in the field may have been exposed, researchers at CaridianBCT Biotechnologies have created a portable system that uses Mirasol™ and UV light to inactivate bacteria, viruses and parasites. The process induces a chemical reaction within pathogens' nucleic acids which renders them unable to replicate and cause harm. The donor's white blood cells that could cause immune complications in the transfusion recipient are inactivated. With TATRC support, the whole-blood system is in its first US human clinical trial as part of the FDA approval process for use in the United States.



A new portable system uses Mirasol™ (riboflavin) and UV light to inactivate disease-causing organisms in donated whole blood.

Large Scale Disaster Response

April 21, 2009

The April Large-Scale Disaster Response PLR consisted of 10 projects within the TATRC Disaster Management, Response, and Countermeasures Portfolio. Projects presented ranged from assessments and mitigation strategies for risks associated with healthcare facilities during pandemic and other disaster events, to worldwide best practices for handling mass casualty events in military and civilian hospitals, and response strategies for complex medical emergencies and disasters. While many of these projects mainly focused on the preparations and management of disaster events from the context of providing healthcare services and sufficient and effective surge capacity, other projects focused on using modeling to simulate infectious disease spread and resulting response. Taken together, the projects of this Portfolio comprise an important integrated approach of advanced technologies in practical application at those times of greatest need.

Geographic Utilization of Artificial Intelligence in Real-Time for Disease Identification and Notification (GUARDIAN) System Knowledge Enhancement Project

Geographic Utilization of Artificial Intelligence in Real-Time for Disease Identification and Notification (GUARDIAN) is a real-time, scalable, extensible, automated knowledge based biological threat agent (BTA) detection and diagnostic system. The purpose of GUARDIAN, being developed by Pangaea Information Technologies and Rush University Medical Center, is to conduct real-time analysis of multiple pre-diagnostic parameters in order to improve the clinical sensitivity to detect disease occurrence from specific BTAs. The goal of the system is to assist clinicians in detecting potential BTAs a quickly as possible based on these pre-diagnostic data in order to prevent a large scale outbreak. Until now the system has only included the major BTAs from Category A (Anthrax, Botulism, Smallpox, Viral Hemorrhagic Fevers, Tularemia, and Pneumonic Plague). The refined system will incorporate BTAs from Category B and naturally recurring disease outbreaks such as Brucellosis, Ricin Toxin, Q Fever, Influenza, Malaria, SARS, West Nile Virus, Acinetobacter, and others.

One of the key strengths of this project in the TATRC Biosurveillance Portfolio is that it is directed by clinicians with a great deal of experience in outbreak detection. Many disaster response and Biosurveillance projects are technology focused, this project has sought the relevant technologies for clinical application in this area.

GUARDIAN Interface Components: Real time monitor, Case Detail, Mapping Interface, Alert Notification.

Simulation-based Planning and Training Tool for Infectious Disease Outbreak, i.e., Pandemic Influenza

PandemicWorld is being developed by Total Immersion Software as an aid to hospital and other MTFs in planning for and managing a medical catastrophe. PandemicWorld's purpose is to allow hospital/MTF personnel to develop and evaluate operational plans for resource management (personnel, traffic, triage, treatment management) in their own unique treatment facility across a variety of operating conditions. Conditions include controlling the rate and mixing the influx of patients (i.e., pandemic flu victims or people with everyday needs such as accident victims, women going into labor, etc.), the availability of health care workers, and the availability of resources.

PandemicWorld provides a look-ahead capability that will enable hospital planning personnel to predict how conditions in their unique facility will unfold in the event of a medical catastrophe. This will enable creation of disaster plans with much greater detail and value which will, in turn, enable hospital operations to be maintained at a higher level of performance than would be possible without the tool.

In addition, PandemicWorld's simulation capability can be used as an architectural simulation tool during hospital design to optimize the operational characteristics of the physical space and processes within the facility.

Simulation-based Planning and Training Tool for Infectious Disease Outbreak, i.e., Pandemic Influenza

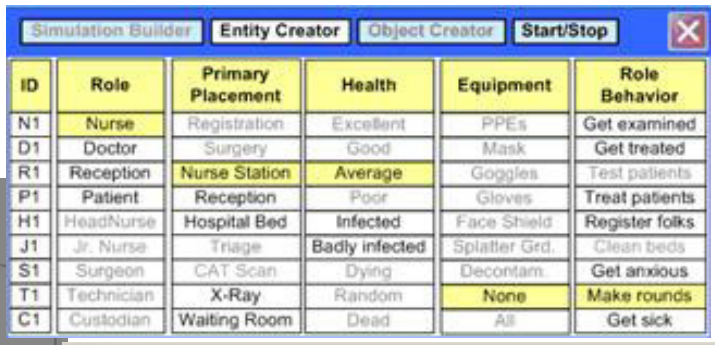
Medical experts and public health officials agree that the nation is overdue for an infectious disease outbreak, most probably of pandemic influenza. It is critical that MTF personnel have the opportunity to practice developing and deploying plans prior to an actual pandemic. In their Phase II effort, SimQuest International, LLC, will develop a prototype for a strategic simulation-based game that will allow MTF administrators and supervisors to understand the causal relationships that strategic planning and tactical decision-making have on the spread of disease, thereby enabling them to respond quickly and effectively.

The proposed Phase II work culminates in a prototype of a PC-based real-time strategy game that will evaluate users' ability to recognize early warning signs, track their strategic planning and decision making when presented with actual events, and allow practice of mitigation strategies at the local level—which will likely reduce the spread of disease in the event of pandemic influenza.

Anticipated results of the Phase II effort include incorporation of scientific pandemic models into a game engine environment and development of a game/simulation in which MTF administrators can train for, experiment with, and experience the realities of a pandemic influenza outbreak. This will give them the knowledge and experience they need to successfully respond to a real outbreak, thus mitigating the spread of the disease as well as its human and economic effects.

These two SBIR programs were created as part of an overall Pandemic Planning program that started at the Office of Naval Research (ONR) around 2005. The ONR program, created a simple tool using the CDC pandemic models in a military logistics

Next functional prototype for key GUI and path navigation tests.



"wrapper" to project casualty rates and logistic impact of pandemic influenza. At the same time, ONR initiated a research program to model disease spread on Navy ships.

Based on discussions with TATRC program managers at the time, the decision was made to initiate an SBIR program that would investigate what could be done to use videogame technology to create a similar simulation system that would assist in hospital planning and training for pandemics and decided to seek funding thru the SBIR program.

Disaster Preparedness and Response Informatics Workshop, April 22-24, 2009

This joint UTHSC-TATRC workshop focused on the assessment of informatics needs for a more efficient and effective model for preparing for and managing emergency medical services and health systems during mass casualty disasters with added emphasis on persons with medical special needs. The goal was to initiate and provide a forum for discussions regarding informatics needs to support new strategies for disaster preparedness, existing infrastructure limitations, future approaches to integrating information technology and the development of cross-functional synergies amongst public and private agencies. It was anticipated that the Workshop would facilitate the development of new ideas and relationships as we pursue optimized medical crisis response services supported by an integrated information system. In addition to these broad goals, projects from government, academia, and industry were presented and highlighted a number of relevant projects with the TATRC-funded Disaster Management Portfolio to establish a framework and process and stimulate collaboration. Also, a UTHSC community demonstration project for health information exchange had been developed and presented. The goal of the pilot project is to identify and enroll 10,000 individuals with Medical Special Needs into this pilot informatics project. Opportunities for using real time surveillance, hand-held/mobile computing, data integration/synthesis for situational awareness and how to integrate them into existing emergency management systems will be explored.

Disaster Health Information Exchange Workshop, December 2-4, 2009

This was the follow-up workshop to the April Disaster Preparedness and Response Informatics Workshop. The goals of this Conference were to:

- Debrief from the Fall American Recovery and Reinvestment Act (ARRA) and other funding efforts to define lessons learned for future initiatives for the State of Texas.
- Establish an opportunity for local and state planning dialogue including disaster preparedness for statewide use cases.
- Establish the opportunity for planning among local and state HIE and Regional Extension Centers to assure use cases including disaster informatics.
- Define research and educational needs for HIE and Regional Extension Center (REC) constituents.
- Develop a framework for future policy development at the local and state levels.

And was attended by nationally-recognized researchers in HIT, State policy makers involved in recent grant activities and related groups, Health Information Exchange (local and state) stakeholders, and Regional Extension Centers and Partners.

PLRs in the News

All of the PLR-related news articles by TATRC science and technology writer Barb Ruppert were approved for Army and other use. They were submitted for publication in military media as well as in the Frederick News Post and the researchers' local media outlets. All can be found at www.tatrc.org in the "Library" section.

TATRC's PLR Report Summary Articles

May 19, 2009 - Soldier Mounted Eye-Tracking and Control Systems: Eye-Com Biosensor, Communicator & Controller

June 23, 2009 - ABO/Rh Forward Typing for Efficient Donor Screening

June 23, 2009 - Transportable Pathogen Reduction Blood Safety System

June 23, 2009 - A Multi-Purpose Sprayable Liquid Wound Dressing for the Far-Forward Battlefield Stabilization of Injury, Pain, Infection, Bleeding & Hemorrhage

July 10, 2009 - 101st Army Airborne Injury Prevention and Performance Enhancement Program

July 28, 2009 - Three Projects from Infectious Disease Portfolio

August 5, 2009 - RenaStick: A Rapid Urine Test for Early Detection of Kidney Injury

August 18, 2009 - Advanced Bioengineering for Soldier Survivability Eagle Tactical Athlete Injury Prevention/Performance Optimization Program

September 1, 2009 - Medical Imaging Software Framework for Rapid Development and Clinical Interoperability

A key gap exists between R&D and implementation of new products and concepts. What is often lacking is an early demonstration of how new technologies might actually work in a specified environment. The AAMTI and Operational Telemedicine programs are TATRC creations that receive non-research Army funding each year to help bridge this gap. AAMTI targets clinical process improvements in medical treatment facilities which are not addressed by any other type of funding. Operational telemedicine supports demonstrations in the field, primarily in the Combatant Commands (COCOMs) and in support of their stability operations and humanitarian missions. This program has also seeded some very important Army initiatives such as Army Knowledge Online (AKO) Teleconsultation, the AMEDD telehealth network, and the tele-TBI cell phone and Transcranial Doppler (TCD) initiatives; additional operational funds have been received for these programs after their importance and feasibility became apparent.

TATRC has also leveraged the SBIR/STTR program to develop discrete technology solutions through small business inventors that address critical DoD gaps, particularly in under-resourced program areas. In the past decade, this program has been used by TATRC to address medical training systems, health information technology, nano-medicine and biomaterials science, medical robotics, and advanced prosthetics—all programs where no core research programs existed. Some of the representative successes are highlighted in this section.

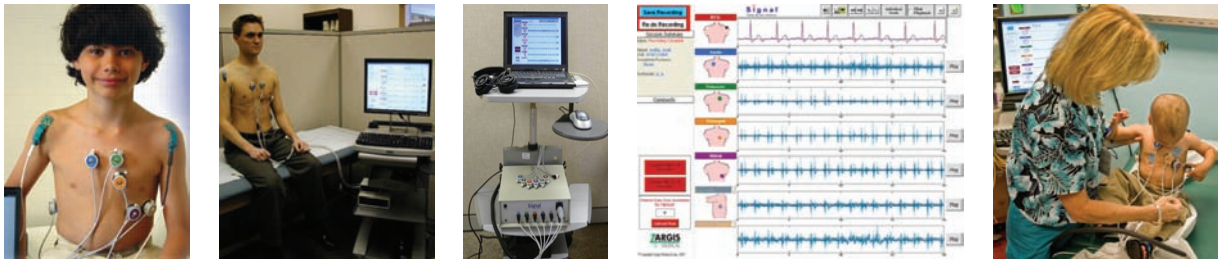
AMEDD Advanced Medical Technology Initiative (AAMTI)

The Army Medical Department (AMEDD) has many unique challenges differentiating it from the civilian medical sector, such as rapid mobilization of military medical assets, providing emergency care on the battlefield, and providing rehabilitation to Soldiers recovering from multiple, devastating injuries. AMEDD must meet military mission requirements while providing quality care to retirees and beneficiaries, demanding the demonstration and adoption of innovative solutions. As the intersection of technology and medicine broadens a focused method of identifying and demonstrating technologies and their impact on the cost of, access to, and quality of, care becomes imperative. Recognizing this, in FY99 the Army Surgeon General, through TATRC at USAMRMC, provided $5M for the AAMTI. The AAMTI was developed to provide AMEDD personnel funds to demonstrate specific technologies in an AMEDD setting.

The AAMTI program supports the comprehensive mission of the USAMRMC which is to provide solutions to medical problems of importance to the American Warfighters at home and abroad. In addition, this program supports and enhances TATRC's management of projects funded through Congressional Special Interest, Small Business Innovative Research, and other programs by providing an opportunity to demonstrate technologies developed through these programs in a military-unique setting. The AAMTI also supports TATRC's technology transfer efforts as a first step in identifying a technology's potential military relevance as demonstrated by potential AMEDD stakeholders and customers.

The scope of the AAMTI program includes identification, exploration and demonstration of key technologies and enabling biomedical principles required to overcome technological barriers that are medically and militarily unique. In addition, the AAMTI provides three important benefits: demonstration of advanced medical technologies and their impact on cost, access and quality of care; provides senior AMEDD leadership with medical tech-watch capability; and encourages medical technology entrepreneurship by funding AMEDD technology innovators.

Problem: Pediatric Telecardiology Referrals with Echocardiographic Validation



AMEDD Advanced Medical Technology Initiative

2004	2005	2006	2007	2008
Pacific Rim Pediatric Heartsounds Trial: Store and Forward telecardiology with echocardiographic validation	Pediatric Multi-site Phonocardiography: Automated interpretation of pediatric heartsounds	Simultaneous Multi-site Phonocardiography: A simplified heartsound	Improved heartsound signal analysis using simultaneous multi-site phonocardiograms in children	Telecardiology evaluation of newborns with heart murmurs using simultaneous, multi-site phonocardiography

From 2004 through 2008, the AAMTI program funded the development of an FDA approved device that works with the Pacific Asynchronous TeleHealth system at TAMC. This device allows for pediatric cardiologists to consult with general practitioners from all of the Pacific region medical centers regarding pediatric heart disease, reducing the cost of referrals and patient transport, and improving access to specialist care.

Representative successes of the AAMTI

Tele-pathology:
Is currently employed at all six Army Regional Medical Commands.

Paperless Flight Physical Exam (AERO):
A web-based system that allows on-line creation, approval, and archiving of Army flight crew physical exams. This robust platform has reduced approval and processing times from 180 days to less than three days developed by the United States Army Aeromedical Research Lab.

Firearm Training System (FATS):
A simulated firing range developed to support Service Members with amputees. The project was initiated at Walter Reed Army Medical Center.

Multi-Site Phonocardiography:
A robust and portable pediatric heart-sounds system. This technology integration program was created by MAJ (P) C. Becket Mahnke, the University of Hawaii and Zargis Medical Corp. A commercial product is currently being developed.

Tele-dermatology:
AAMTI provided funding for studies that proved the case for the adoption of tele-dermatology. Program funds were used to provide supporting data critical to the acceptance of tele-dermatology in the AMEDD.

Cell Phone System for Diabetes Management:
A Comprehensive Diabetes Management Program at WRAMC to demonstrate the efficacy of delivering patient reminders and lifestyle information via cell phone. As a result of this study, the AMEDD is exploring cell phone-based patient care in a number of clinical and health care areas, to include TBI and PTSD.

Tele-echocardiology:
AAMTI funded studies of real-time and store-and-forward tele-echocardiology systems. The studies identified obstacles to the employment of each type of system as well as benefits dervived from each.

Speech Recognition:
An early AAMTI study conducted in 2000 looked at the state of speech recognition in the commercial sector with an eye towards incorporating such a capability in the AMEDD for physician entry of clinical data. The study showed that the commercial sector, at that time, had not solved technical problems with such a system and recommended that AMEDD leadership not direct significant funding to speech recognition technology.

Common Development Environment (CDE):
The CDE is a mirror copy of the Armed Forces Health Longitudinal Technology Application (AHLTA). AHLTA is the military electronic health record and AAMTI funding helped to establish the CDE that allows new functionalities to be demonstrated without disrupting the live system.

Tele-chemistry:
The AAMTI funded a study of the use of tele-maintenance technology to inspect and calibrate sensitive chem-bio detection equipment from a distance. Given the high cost and danger associated with sending contract personnel into a war zone, this project assessed some of the problems and issues arising from the use of tele-maintenance and made some suggestions as to how such a system could be standardized.

From the period of 2000 to 2007, approximately 175 projects were funded, Many of the key findings have been published and the ensuing recommendations and follow-on demonstration efforts have been implemented. The AAMTI has led to seven years of discovery, productive technology demonstration, and advances in military medical technology.

The AAMTI is a valuable, bottom-up approach to identifying and demonstrating technology that may have an important impact on military medical care. As care providers and patient administrators increasingly incorporate technology in their practice it is imperative that they be provided access to the technologies that will provide a flexible model for improving medical care.

Operational Telemedicine

The four main initiatives during 2009 were the AMEDD's Regional Medical Center (RMC) telehealth; mCare (formerly known as the Tele-TBI Cell Phone Initiative); and the transcranial Doppler (TCD). Proposals were submitted in September 2007 and the projects were approved in February 2008. Money was received for all three initiatives in FY08 (RMC telehealth received $8.5M to include equipment and personnel, and about the same amount is projected for personnel in FY10 and subsequent years; mCare received about $1.9M in FY08, which will be sustained by $1.3M in subsequent years as the program expands to include up to 10,000 Warfighters; and TCD received over $1M in FY08; and will need about $800K for each of the outlying years). TATRC personnel have worked closely on all of these initiatives with individuals from the Office of the Surgeon General's (OTSG) -Health Policy and Services PTSD and TBI, Propoency for Rehabilitation and Reintegration Offices, and the RMCs' designated personnel.

These initiatives address the needs of Service Members who have been identified with having mild to severe TBI and reach out to where the Service Members work and live, as well as, to where they are being treated. For the most part these initiatives are minimizing the need for the Service Members and providers to travel to receive and render care; enhancing communication between Service Members and their caregivers in a manner that today's Soldiers prefer; obtaining quicker assessments; and ultimately affecting the outcomes in a positive way. This program also supports many international health/COCOM telemedicine activities.

The teleconsultation program utilizes the most current knowledge about telemedicine to provide specialist consultations to our medical personnel in the field, while taking into account the clinical, privacy, and bandwidth issues involved.

AKO Teleconsultation

In April 2004, the US Army, with the active involvement of TATRC, initiated a teleconsultation program for the use of deployed forces. The intent was to utilize the most current knowledge about telemedicine to provide specialist consultations to our medical personnel in the field, while taking into account the clinical, privacy, and bandwidth issues involved in this type of teleconsultation. The system makes use of routine internet access and providers' personal digital cameras. Consultants are on a call roster, and respond to requests for support 24 hours per day, every day. Deployed worldwide, with primary users being in the Middle East, the Balkans, Iraq, and Afghanistan, this system has been highly successful and is well-accepted, with more than 5,700 completed consultations through June 2009. Consultations are available in 19 specialty groupings, and have prevented 74 unneeded evacuations, facilitated 220 evacuations from theater, and provided timely assistance to thousands of our deployed personnel.

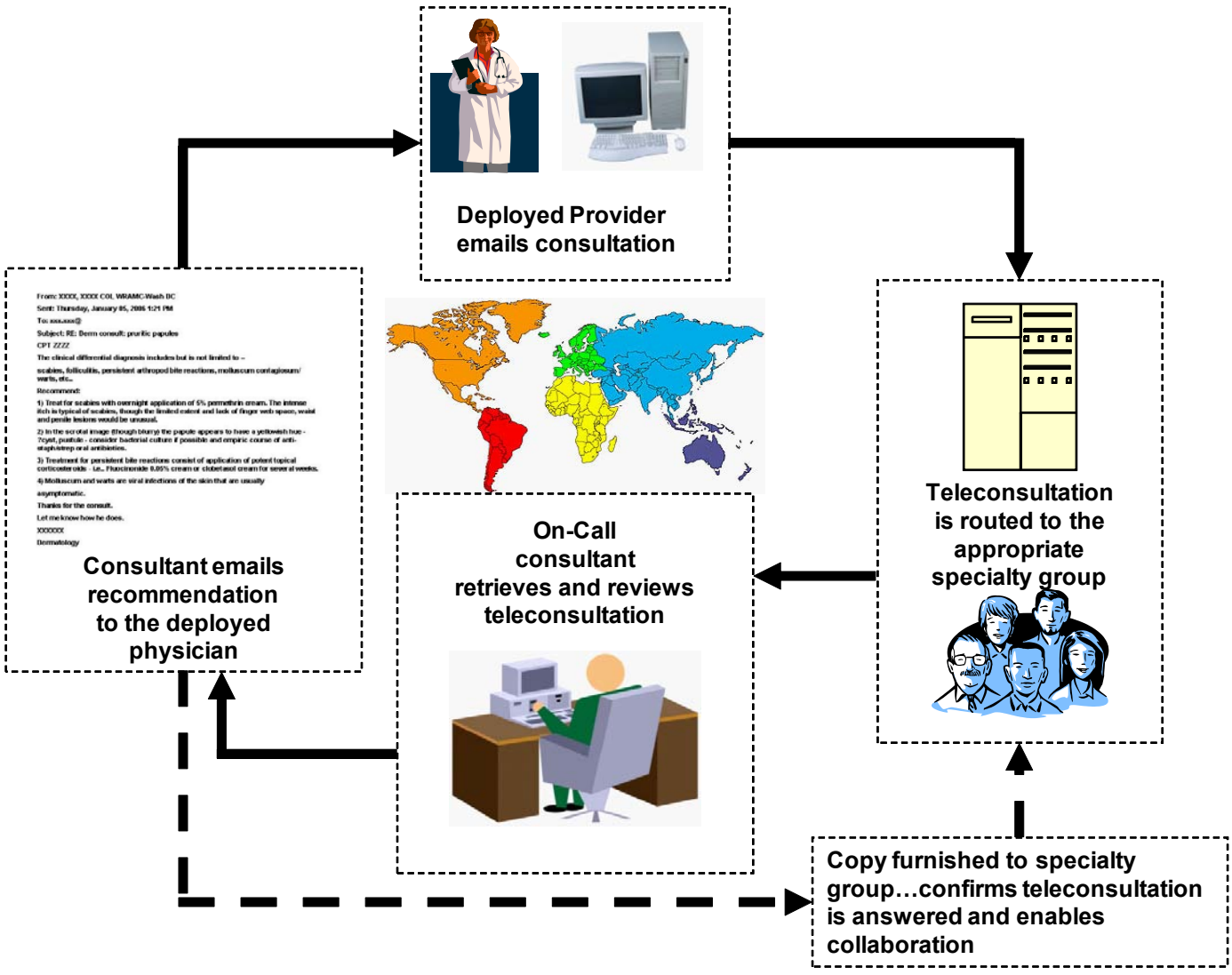
One of TATRC's efforts under the Operational Telemedicine Portfolio, has been to continuously assist our NATO Allies implement and improve their own national military telemedicine programs. The goal has been to assist them in development and standardization of systems to support coalition medical support operations. TATRC has continued to play a major role in the NATO Telemedicine Expert Panel, and the AKO Teleconsultation system has been used as an example of a working system. As a result, most allied nations now have some version of a teleconsultation system, though most are not as fully functional as the Army Knowledge Online (AKO) system. With NATO's increased involvement

in operations in Afghanistan, consideration was given to development of a NATO system for teleconsultation, but the recommendation within NATO channels was to attempt to utilize existing national systems rather than to develop new NATO systems. Accordingly, the Committee of the Chiefs of the Military Medical Services in NATO (COMEDS), the most senior medical body in NATO, requested that deployed NATO-led forces in Afghanistan be authorized to use the consultative capabilities of the Army system, at least on a temporary basis.

After coordination of US support, TATRC led the way in developing an agreement between NATO's Allied Command Operations and the US Army's Medical Command. After full staffing in both NATO and the United States, the MOU was signed in October 2008. TATRC contact teams were sent to the theatre to brief potential NATO users soon thereafter, and NATO usage started in February 2009. The program has been well-accepted, with 24 consults from NATO forces in 10 specialty areas managed through the end of June 2009. One nation which has been using the system is so impressed that their Surgeon General has requested that they be allowed to use it to support all their deployed forces worldwide.

The US Army/NATO agreement is materially benefiting Warfighters in Afghanistan and is an excellent example of the transition of TATRC efforts from research to field use.

Teleconsultation Program Business Practice



AMEDD's RMC Telehealth Network

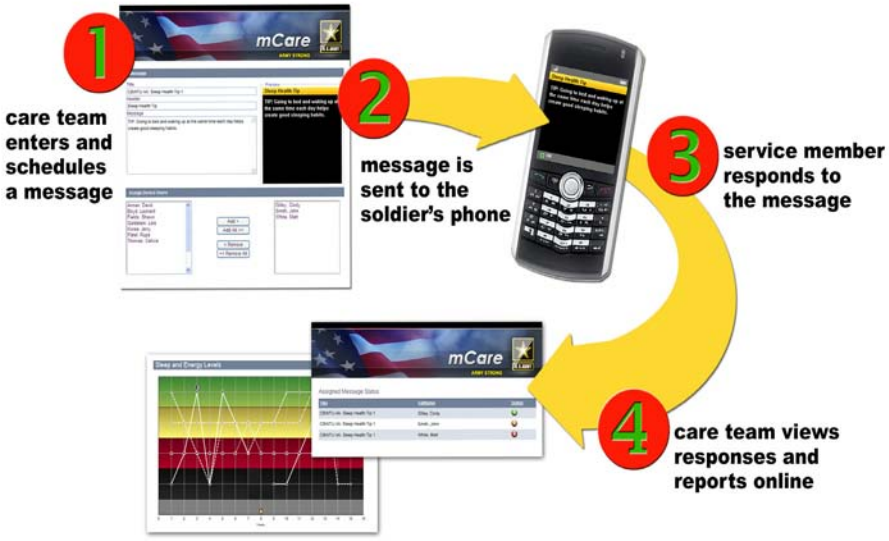
A U. S. Army-wide telemedicine network has been established to meet the evolving clinical needs of a geographically dispersed military population. Five RMCs spanning 14 time zones – from American Samoa to Germany – were identified and personnel and equipment needs procured based on clinical needs. In phase 1, a centrally managed RMC Management Teams (13 people in total) consisting of a tele-TBI program manager, clinical and technical advisors were put in place at the five RMCs to help build their programs and develop policies and procedures. Site surveys, clinical, technical and administrative assessments were conducted for all five RMCs. More than 60 sites have been equipped with video teleconference (VTC) equipment and it is estimated that this number will increase to over eighty in the coming months. Over 15 different medical disciplines conducted telehealth encounters. As of September 2009, greater than 17,000 behavioral telehealth and tele-neurosurgery encounters were conducted in fiscal year 2009. It is anticipated that we will see a dramatic increase in telehealth encounters in 2010 for other clinical disciplines as we augment the current medical treatment facilities (phase 2) with 63 additional clinical, administrative and technical personnel. Teleconsultation clinical models such as behavioral health, neurosurgery, headache evaluation, neuropsychology, speech and language pathology were established and others such as, orthopedics and neurology are being developed. The neurosurgery teleconsultation program return on investment alone was over $2M in 2009.

Telemedicine will continue to increase access to care, reduce patient and specialist travel, decrease lost work times, return money to the medical command by avoiding clinical referrals to the civilian sector and was widely accepted among the patient population. TATRC has initiated the documentation of metrics such as, the number, type and location of telehealth encounters; cost avoidance by conducting a telehealth visit versus a face-to-face visit, as well as solicited qualitative metrics. Lessons identified will be shared across the AMEDD with all regional medical commands and with the Army Surgeon General's Post Traumatic Stress and TBI Behavioral Health Integration team.

mCare: A Tele-TBI Cell Phone Initiative

The "m" in mCare stands for mobile. The mCare platform allows care coordination for Warriors in Transition utilizing an encrypted, bidirectional messaging system. The system conveys information directly to a HIPAA compliant application installed on the Soldier's personal cell phone. Messages sent through mCare currently include: appointment reminders, unit announcements; health and wellness tips, and resource messages. mCare messages are scalable; they can target every enrolled cell phone participant, specific geographic regions, units, or individual patients.

Soldiers interact with mCare in a straightforward fashion, they simply respond to messages by selecting a button or single character. These replies are returned securely, to the online mCare portal. This web site is the conduit for the care team to send messages and review patient feedback. As the project



mCare is a four part process: 1. The care team enters web site and schedules a message; 2. The message is sent to the Soldier's phone; 3. The service member responds to the message; and 4. The care team views responses and reports online.

matures, and when necessary, the care coordination staff receives e-mail alerts from the mCare system.

The mCare initiative was funded jointly by the OTSG and USAMRMC Health Force Protection. OTSG funding has supported the initial infrastructure, staffing, pilot testing and performance improvement evaluation efforts. USAMRMC HFP funds are driving a rigorous research study evaluating administrative, clinical, technical and system outcomes of mCare.

TATRC is leading a multi-disciplinary partnership to achieve mCare's goals. The following government and academic organizations have also participated in the development of the mCare concept: Afterdeployment.org; Army Office of the Assistant Secretary of the Army Manpower and Reserve Affairs; DCoE, DVBIC, Government Printing Office, USAMRMC, OTSG PR&R; North Atlantic Regional Medical Command (NARMC); Sister Kenny Research Center; Southeastern Regional Medical Command (SERMC); and the Warrior Care and Transition Office. The mCare initiative has also been enhanced with services from industry, including: AllOne Mobile; AT&T; Clickatell; Diversinet; National Software Testing Labs (NSTL), Qualcomm, Sprint NEXTEL, T-Mobile and Verizon. These multidisciplinary partners have been separated into four distinct tiger teams in the areas of technical, clinical, research and oversight that meet weekly to shape the direction and focus of the project. These virtual teams have been collaborating since fall of 2008 through teleconferences, a designated set of web portals, workshops and offsite meetings.

Addressing the challenges of coping with memory issues associated with TBI is exactly why mCare was developed. Patients like this will be followed throughout both phases of the project to ensure that this technology solution is a value added to their quality of life, and quality of care in the future.

Another key feature of mCare was provided dedicated staffing to the initial five participating sites. Registered nurses called Project Liaisons who are trained on the use of the mCare application are working side-by-side with the entire Community Based Warrior in Transition Unit (CBWTU) team including participating case managers, social work-

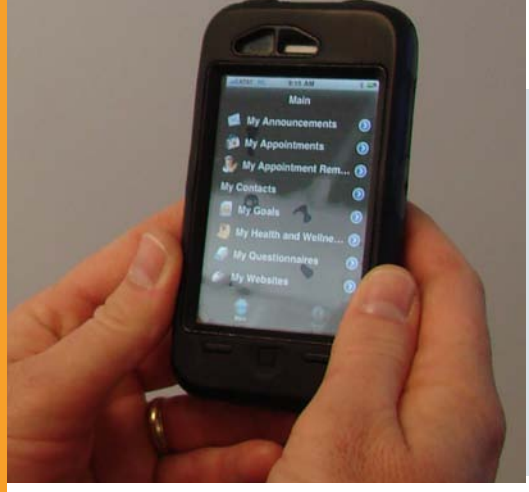
One Soldier's Story

A wounded Warrior assigned to the CBWTU in Massachusetts was struggling with memory issues related to his TBI. He frequently forgot about upcoming appointments, and as a result, was not receiving care as he should. His coordination team was concerned that he might not be able to continue to recover at home if a solution could not be found to assist him in getting to his appointments. Since being assigned to a CBWTU is a privilege, this patient was in jeopardy of not being able to continue with the program.

The Soldier's platoon sergeant was the first to suggest that mCare might be a good solution for this patient. When the mCare project liaison contacted the individual by phone, he told her that he was trying very hard to remember his appointments. He always wrote down the dates and times to keep them in his pocket. Unfortunately, he would then forget that the note was in his pocket, and would wash his clothes before removing the reminder notes. He needed continual reminders in a way that would always reach him.

Because of his challenges with finding a way to keep himself on track, the wounded Warrior was open to having mCare installed on his personal cell phone. However, his phone was not one of the model supported by the initial release of the mCare software. But he volunteered that he thought he might be eligible to upgrade his phone.

With the Soldier's permission, the project liaison then engaged the local Verizon office in the patient's home community to determine if a solution could be found. The wireless provider was able to provide the solder with a compatible phone upgrade that he found acceptable. With over the phone instructions, the mCare application was downloaded to this patient's new phone, and he was receiving and acknowledging reminder messages before he even left the phone store.



The mCare phone application requires a 6-digit pin for secure access. Within the mCare application, a patient can access messages that include: announcements; appointment reminders; health and wellness tips; and questionnaires. Additional resources include care team contact information and recommended web links.

ers, platoon sergeants, medical directors and unit leadership to find the best means of utilizing mCare throughout both phases. The end goal is to leverage these staff to migrate the use of mCare into everyday practice by the unit staff over time, thus negating the need for permanent full time employees.

There are two initial phases to the mCare project. There is a performance improvement project that is currently underway and a randomized, controlled research study that will commence in the fall of 2009. There are currently five sites participating in the mCare initiative. They are all CBWTUs, which are specialty units that allow the outpatient wounded Warriors to receive care in their home community, rather than on a military installation. The care team located at the CBWTUs are geographically separated from the patients, in some instances by several hundred miles. They remotely follow all of their patients by telephone daily for administrative issues and weekly for clinical follow up. The CBWTU sites currently participating are located in Alabama, Florida, Illinois, Massachusetts and Virginia. Considering the interest and positive feedback received to date, mCare may be expanded to all 9 CBWTU sites within the US Army. Additionally there is interest in exporting mCare to traditional WTU sites within the Army and Navy. Finally, it is anticipated that mCare will soon migrate to the VA as a selected pilot to achieve a seamless transition model. The capacity of the mCare infrastructure is 10,000 cell phone users.

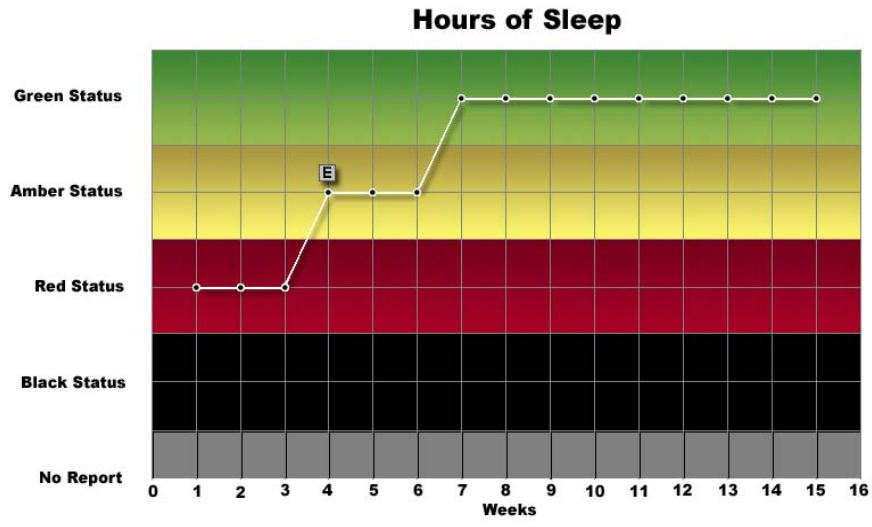
The design and development of the mCare technology platform was driven by four major factors: security and privacy; availability across the spectrum of wireless devices used by the general public; ease of use for the patient; and direct and simple access for the healthcare team members. It was critical that the mCare technical infrastructure provides secure information exchange between the Wounded Warrior and the care team. Patient privacy was of the upmost importance for this effort, standards established by the Initiative for Open Authentication (OATH), Internet Engineering Task Force (IETF) and RSA public key cryptology are all included in the security requirements and were a driving factor in the project vendor selection criteria. Every aspect of the data storage and exchange were critical aspects to the system design, but particular focus was directed on the information flow to and from the cell phone. As a result, SMS communications, or unsecured text messaging, are only used to prompt the patient that information was now accessible through the secure mobile phone application. All personal and health related information was transmitted to and from the patient's cell phone using transport layer security (TLS)/secure socket layer (SSL) and an application layer securing protocol using dynamic 192-bit encryption keys. As a result of the mCare secure communications structure, the mobile devices must be capable of both text and data services, also known as a media capable phone.

The service member accesses the mCare messages with a six-digit PIN code, known only by the end user. This PIN code serves as one of the two factors of authentication on the mobile device; the second is soft token security. Personal heath information (PHI) or personal identifiable information (PII)

provided by the patient back to the mCare server is stored on a secure vault appliance within the computer security demilitarized zone (DMZ).

The second phase, research effort will be limited in scope to the initial five CBWTU sites, and will have expanded clinical functions. The research study is planned to be nine months in duration, with up to 400 participants. The research study will feature the ability to query and review each patient's weekly status over time for multiple categories like pain, mood, energy, sleep, interpersonal relationships, and general wellbeing. The graph below depicts responses to questionnaires sent forward to the mCare web interface in a graphical representation over time. The care team at each of the participating research sites will have this same capability with mCare for each of their participating patients.

In June 2009, mCare launched its phase 1 effort, and currently has 80 active cell phone users. The target for the phase 1 effort is to enroll 100 patients and evaluate their use over three month intervals for the next year. Active enrollment is continuous, therefore and reaching and exceeding this goal is expected to occur in the fall of 2009. Data collected over the first 3 months use of mCare has show a high message delivery rate (over 90%), and an high response and/or acknowledgement rate of nearly 80% by all participants. To date, over 6,000 messages have been sent using the mCare infrastructure.



Responses to mCare questionnaires can be accessed in a graphical format over specific time periods. This allows the care team to determine if the patient is maintaining, improving, or declining with respect to many case management assessment tools, including pain management, mood, and energy and sleep. This information allows the care team to determine priorities for follow-up based on weekly patient feedback.

In an initial user survey participants reported

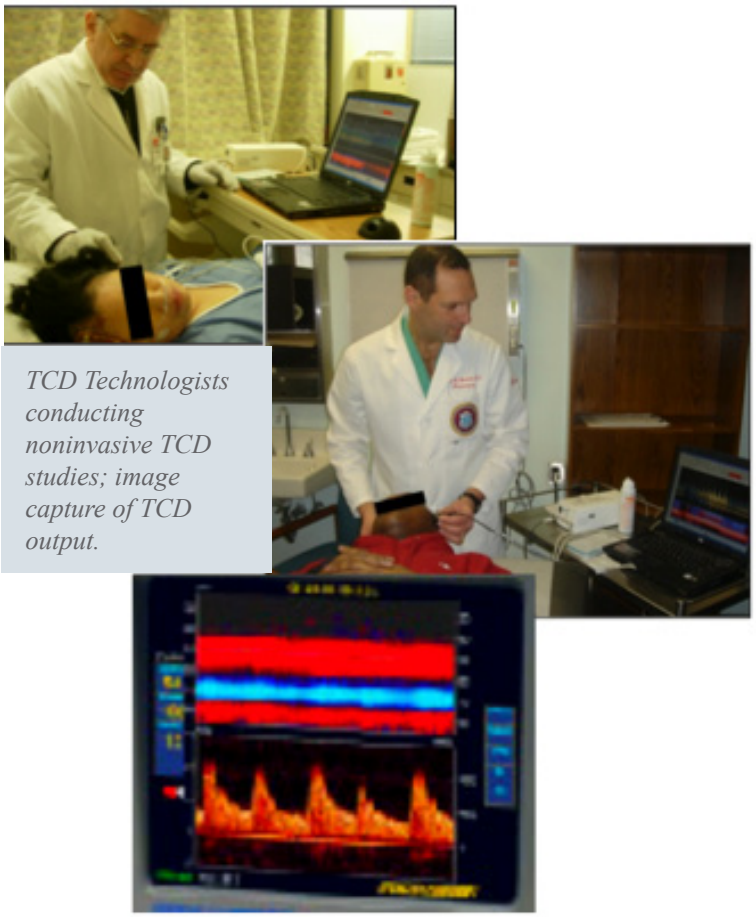
- Over 75% of responders found mCare easy to use.
- Over 90% of users found the health and wellness tips sent through mCare to be helpful and relevant to them.
- Nearly 85% of users reported that they would find appointment reminders helpful.
- When presented with the option of receiving unit information via mCare, e-mail, or both, the majority of patients surveyed preferred both.

In FY10, phase 1 enrollment and data collection will be ongoing to complete the performance improvement objectives. The research study will commence this fall, and will be limited to the five initial sites. Simultaneously, evaluation of mCare for use with larger populations, including WTUs, sister services, and the DVA will be a focus in the upcoming year. Expansion of the initial mCare application with new web-based features, links to wireless application protocol (WAP) and rich site summary (RSS) resources and evaluation of cross-over integration with social network resources are also future endeavors for mCare.

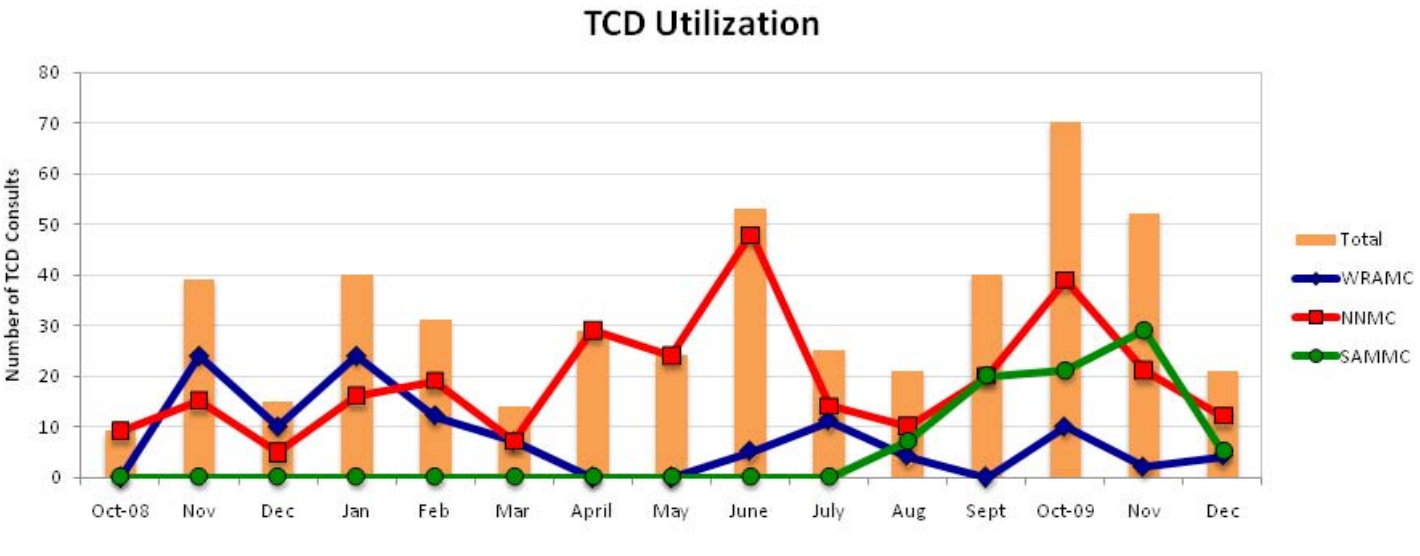
In conclusion, mCare has achieved many significant milestones in FY09, and anticipates a rich quantitative data analysis of the value of mobile phones to engage patient in the military healthcare process in the years to come.

Transcranial Doppler (TCD)

Over the past five years, approximately 30% of severe wartime TBI patients experienced cerebral ischemia as a result of the secondary compromise from blast-induced cerebral vasospasm. TCD is a non-invasive technique using brain ultrasound to assess and monitor cerebral vascular activities in order to prevent patients from suffering further ischemic injuries to the brain. The AMEDD TCD Program supports the US Army Surgeon General's TBI Action Plan and is managed by the TATRC. Utilizing a Central Laboratory, the service provides: TCD testing, monitoring, and interpretation, on-site technical support and round-the-clock helpdesk, and training and certification. In 2009, the TCD Program successfully completed both phases of its implementation plan, providing services to WRAMC, NNMC, and the combined San Antonio Military Medical Centers (SAMMC) of BAMC and Wilford Hall, extending a capability where previously not available and truly taking a tri-service approach. Thus far, over 400 TCD studies have been conducted and preliminary quality review data have indicated that the service have contributed to the pharmacological management of 72% of the patients studied, and have indicated and led to further diagnostic procedures in 18% of the patients, without which they would not have gotten further diagnostic testing. This clearly demonstrates the program's utility and impact on the management of neurotrauma.



TCD Technologists conducting noninvasive TCD studies; image capture of TCD output.



TCD utilization across WRAMC, NNMC and the combined San Antonio Military Medical Center.

Small Business Innovation Research (SBIR)/Small Business Technology Transfer Program (STTR)

The SBIR and STTR are competitive programs that allow small businesses to harness their innovative talents, with the incentive to profit from commercialization.

Both programs follow a three-phase process. Phase I is the startup phase, with awards up to $100,000. Phase II awards up to $750,000 as researchers expand on Phase I results and explore commercialization potential. Phase III moves from the laboratory to the marketplace; no SBIR/STTR funds support this phase.

Portfolio	# of PH I Awards	# of Ph II Awards
Simulation and Training Technology	85	26
Health Information Technologies	55	24
Nano-Medicine and Biomaterials	23	12
Medical Robotics	17	5
Advanced Prosthetics and Human Performance	13	6
Medical Logistics	10	4
Resilience & Retraining	9	2
Neurotrauma	8	2
Computational Biology	5	3
Trauma	4	0
Biomonitoring Technologies	3	3
Medical Imaging Technologies	3	1
Psychological Health	1	1

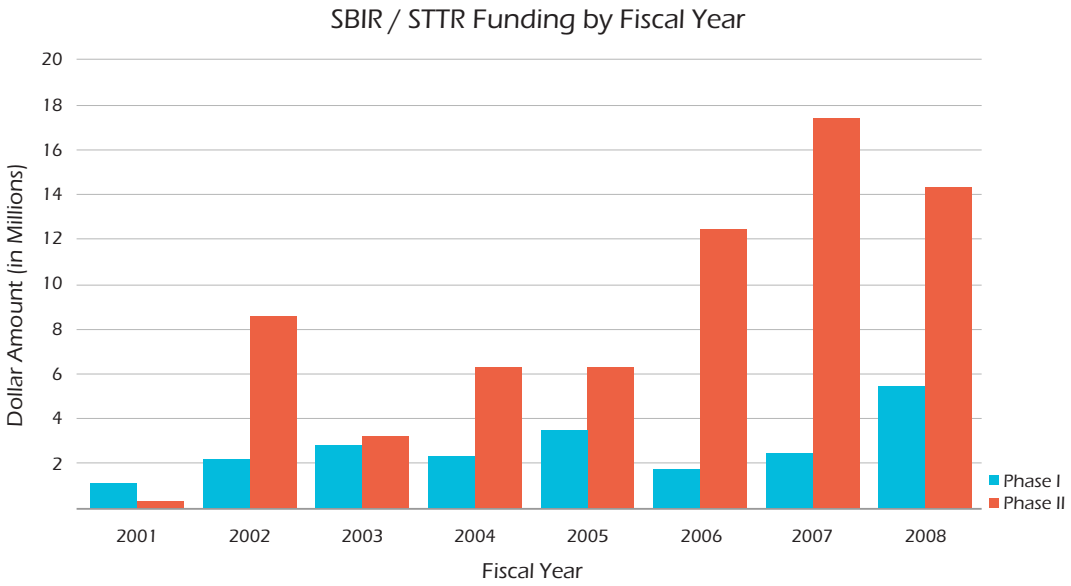
Currently, all federal agencies with an annual extramural R&D budget exceeding $100 million are required to reserve 2.5% for SBIR. Additionally, those federal agencies with R&D budgets exceeding $1.0 billion are required to reserve 0.3% for STTR.

The DoD spends over $1 billion each year on the SBIR program, executed through three yearly solicitations. These solicitations cite R&D needs and invite proposals. Companies submitting proposals must be a US for-profit small business of 500 or fewer employees, work must be performed in the United States, and the Principal Investigator must spend more than half of their time employed by the proposing firm.

Similarly, the STTR solicits proposals from small businesses. However, in the STTR program small businesses are required to collaborate with a research institution (i.e., a university, federally-funded R&D center, or nonprofit research institution). The small business must perform a minimum of 40% of the work and the research institution a minimum of 30% of the work in both Phase I and Phase II. The purpose of STTR is to create, for the first time, an effective vehicle for moving ideas from our nation's research institutions to the market, where they can benefit both private sector and military customers.

TATRC currently authors SBIR and STTR topics and evaluates proposals on behalf of the Army and The OSD. TATRC also provides COR and PO support for awarded projects through each phase.

The SBIR and STTR program has been a very important source of discretionary funding for the DoD to partner with small innovative extramural inventors to provide (dual use) commercializable systems and tools that address specific DoD needs.

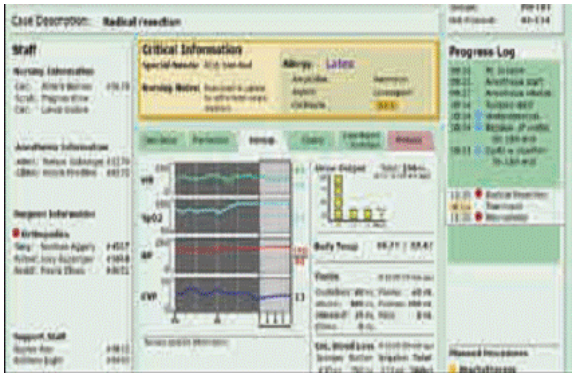


(Fiscal Year does not necessarily correlate with solicitation year. Projects reaching Phase 2 are likely funded in multiple fiscal years.)

Robotic Patient Recovery

Portfolio: Medical Robotics

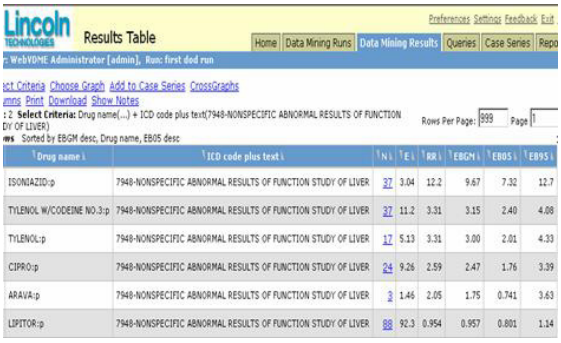
Applied Perception, Inc. designed and prototyped a complete robotic combat casualty extraction and evacuation system to reduce the risk of injury to the combat medic and other rescue personnel when in hostile or dangerous situations. The system consists of a marsupial robotic vehicle pair composed of a small, agile Robotic Extraction Vehicle (REX) for short-range patient extraction from site of injury and a larger Robotic Evacuation Vehicle (REV) for long-range patient evacuation. As a result of developing a complete autonomous system, a wide array of technologies that are applicable to unmanned ground vehicles today were developed along the way. Many of these technologies have either transitioned to other projects or have been marketed and sold outright to other customers.



Patient Safety Perioperative Readiness Support System

Portfolio: Health Information Technologies

LiveData has developed the OR-Dashboard to help the operating room team reduce errors and near misses due to oversight, failure to recognize an issue, and miscommunication. The OR-Dashboard aligns OR processes with hospital strategic objectives, determining whether safety protocols have been followed and flagging the OR team when omissions occur. This addresses an important need in both the military and civilian sectors. The OR-Dashboard is commercially available and has generated over $3.5M in sales and commitments.



Mining Longitudinal Data for Known and Unknown Adverse Events

Portfolio: Health Information Technologies

WebVDME is a visual data mining environment that provides quantitative data analysis and incorporates a signal management module that supports ongoing product risk management efforts. This product has combined with another TATRC SBIR product, developed by Stottler Henke, to become the main software used in the Army Pharmacovigilance Program Office at OTSG. Currently in Phase III, with funding provided by the FDA, Phase Forward is further developing software to enable the mining of longitudinal data for known and unknown adverse events.

GPS-based Tracking System for Trauma Patients

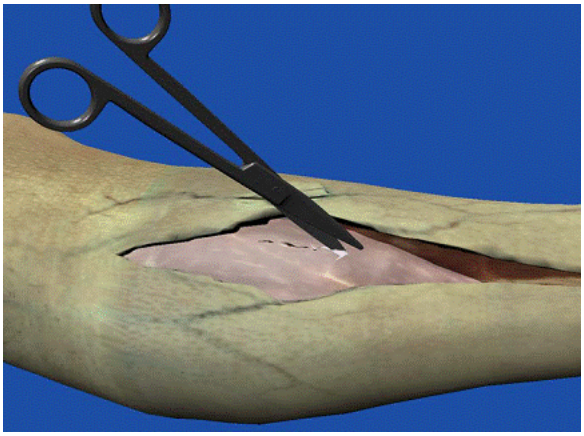
Portfolio: Health Information Technologies

NAVSYS has developed a small form-factor wearable GPS tracking device that could operate for significantly longer periods than conventional, commercial GPS chip sets. This system would have immediate benefit for providing real-time situational awareness of personnel in hazardous areas. NAVSYS has been selected for a Phase III contract award by CERDEC to further develop and verify its technology for an operational military application. Recently, a CRADA was agreed to, establishing a multi-year working agreement that will allow NAVSYS to continue to operate the LocatorNet Server for dual-use tracking applications in support of military and commercial customers.

Compartment Syndrome Simulator

Portfolio: Simulation and Training Technology

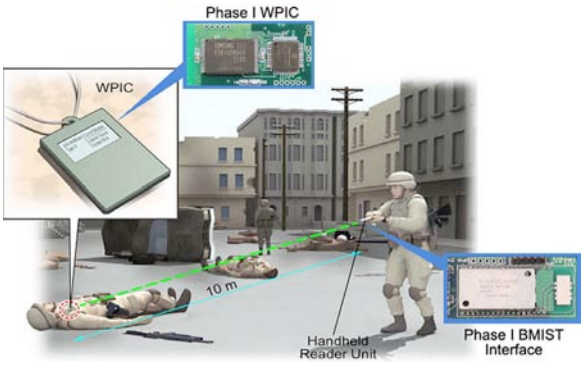
The overall goal of this effort was to create and validate a prototype simulator for practicing the basic skills of diagnosis and treatment related to compartment syndrome. The system uses collocated haptics and graphics to give the user the feel and look of palpation and cutting as related to fasciotomy. An associated Mentor program guides and critiques the trainee's development. This addresses a military need to improve care for Warfighters who sustain extremity injuries and will also have civilian application for orthopaedic training. Touch of Life was the recipient of a Commercialization Pilot Program award and the company has had initial sales success with their Common Platform Simulator.



Wireless Electronic Information Carrier

Portfolio: Health Information Technologies

Wireless Personal Information Carrier (WPIC) technology gives medical personnel instantaneous access and accurate patient medical records without any physical contact. Extending this technology to the general population will simplify record keeping, medical examinations and provides immediate and secure access to medical data in emergencies or normal healthcare use by prioritizing electronic patient records. The WPIC provides wireless read, write, and storage functions, allowing Warfighters and personnel to carry with them 20 years of lossless, encrypted medical records.

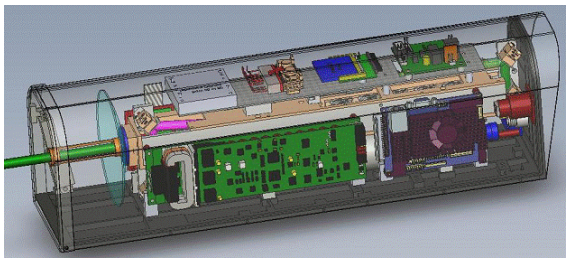


SBIR/STTR Recent Successes

Medical Simulation Training for First Response to Chemical, Biological, Radiological, Nuclear Events

Portfolio: Simulation and Training Technology

Forterra is developing a curriculum and virtual hospital with sufficient medical fidelity to model sick and injured patients in a mass casualty incident, enabling professionals to triage and provide emergency care for virtual patients. This addresses America's need to provide medical first-response capabilities to CBRNE events. Forterra is a recipient of the Army's Commercialization Pilot Program and is expected to receive additional funds from the program.



SUGV-Integrated Non-Contact Deep UV Biochemical Agent Surface Detector (UVBASD)

Portfolio: Nano-Medicine and Biomaterials

The targeted ultraviolet chemical, biological, and explosives (TUCBE) sensor allows Warfighters and first responders to remotely detect and classify CBE agents using a single robot-mounted or hand-held stand-off sensor. It requires minimal training and has no logistical burden allowing expanded utility for many safety response applications. The commercial impact of this technology reaches numerous markets and applications including environmental monitoring, manufactured product quality control in a wide range of industries, and for monitoring the quality of industrial and municipal wastewater, potable water, and agriwater.

Integrated Clinical Environment Manager

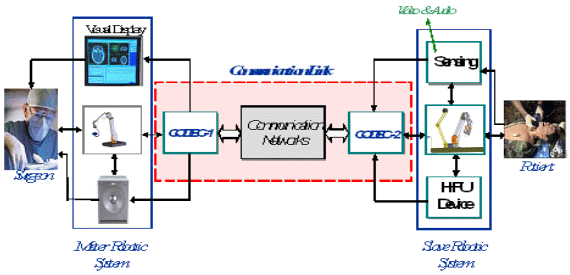
Portfolio: Medical Logistics

LiveData is developing a prototype software system that will use integrated device information, clinical context, and smart workflow-driven notifications to create a safer and more efficient critical care environment. It uses emerging medical communication and Real- Time Integration software to fuse data from medical devices and documentation systems to generate workflow notifications or "smart alarms." These are delivered using Voice-over-Internet Protocol (VOIP) phones, pagers, e-mail, computer "Dashboards" and data feeds. Various civilian and DoD institutions have expressed interest in the product and LiveData has also secured a large commercial partner, Karl Storz Endoscopy, to market the technology.

Smart Codec with Telesurgery Capability

Portfolio: Medical Robotics

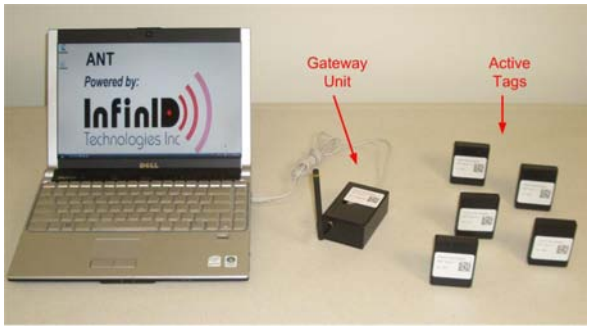
Energid is developing a smart codec device for telesurgery and telerobotics that rapidly adapts to abrupt changes in available network bandwidth, minimizes the impact of network latency jitter, and provides perceptually stable video and haptics. Such performance is critical for real-time system control across battlefield networks and civilian IP and wireless networks. This product will make surgery on wounded Warriors more effective by allowing distant experts to either assist or perform the surgery themselves.



Ad hoc Networked Tags (ANT) for Active RFID

Portfolio: Medical Logistics

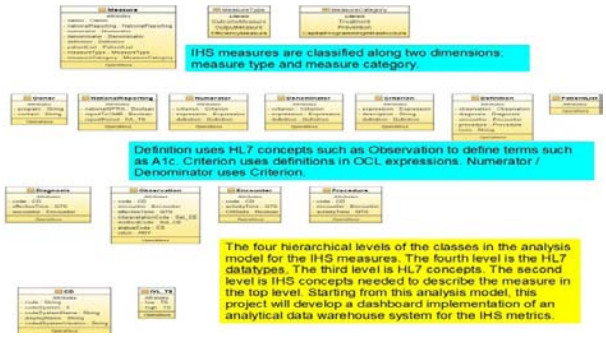
The timely delivery of medical shipments in good condition is necessary to save lives and to alleviate human suffering. In the ANT system, each RFID tag transmits its own ID and sensor readings at very low duty cycle, and also relays readings from other nearby ANT RFID tags, extending the system range and robustness. The data, including temperature, humidity, vibration, and shock, is used for logistics tracking of medical supplies. This will allow replacement supplies to be shipped as soon as a sensor indicates that supplies may be damaged, even before they arrive, and could additionally be used as an inventory tracking tool.



HL-7 V3 Interface Engine

Portfolio: Health Information Technologies

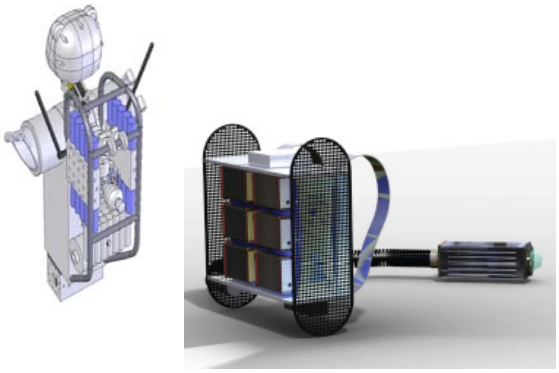
The central purpose of this research project is to investigate the use of HL-7 V3, particularly the Clinical Document Architecture (CDA) Release 2 (R2) as the central basis for developing an interface engine that will provide semantic interoperability. VCR Soft, Inc. has demonstrated conceptually how to add HL-7 CDA concepts to the DoD/VHA BHIE, using open source Mirth components. The work has potential to contribute to the adaptor and enterprise service bus DoD is crafting to connect the FHA gateway to the NHIN to back end military and civilian systems.



Robotic Force Health Protection from Chem-Bio Agents and IEDs

Portfolio: Medical Robotics

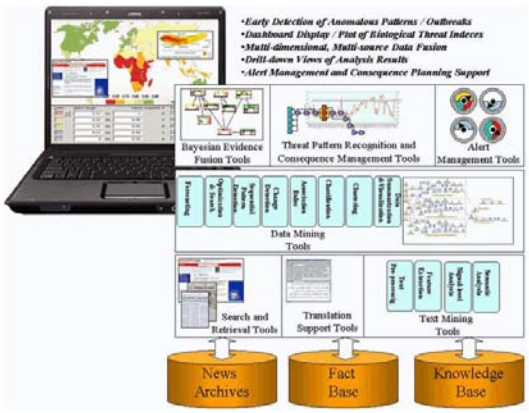
Vecna is redeveloping and deploying a prototype of robotic, unmanned detection system for IEDs, biological and chemical agents and its integration in the BEAR robot. With full integration, this will allow for the detection of hazardous materials without the risk of Warfighter contact. The devices are currently useable on the benchtop and are being improved for use in the field.



Biosurveillance-based Integrated Outbreak Warning And Recognition System (BIOWARS)

Portfolio: Health information Technologies

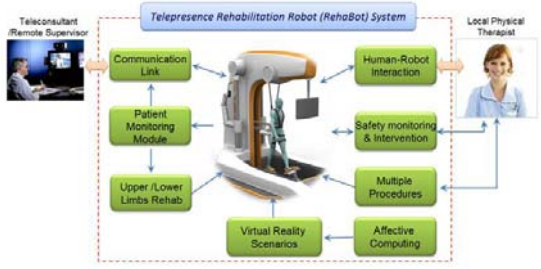
This initiative aims to develop, demonstrate, and successfully deploy a BIOWARS technology as part of a much larger, collaborative effort to enhance our national biosurveillance capability. A prototype biosurveillance community of interest portal has been developed, based on upgrades to the Drupal portal platform and the Blackbook2 platform. The goal is to provide a portal onto the web for medical health professionals and bio-informaticists involved in the detection and monitoring of on-going and historical events throughout the world, with relevance to long-term health prospects. KBSI has established a proof-of-concept design and prototype through which the community can evaluate that architecture. This resource is available to registered users on the web; feedback from those users is helping to shape enhancement and evolution of the prototype.



An Integrated Physical Therapy/ Rehabilitation Robotic (RehaBot) System for Military Healthcare Enhancement

Portfolio: Advanced Prosthetics and Human Performance

The (RehaBot) system will enhance rehabilitation training quality and efficiency for Soldiers and civilian patients with neurological and muscular injuries or functional impairments. To date, Hstar Technologies has designed a RehaBot exoskeleton-like upper limb rehab system and non-treadmill paddle-based haptic feedback ambulatory training system for lower extremity function retraining, as well as an integrated control system suitable for safe and robust rehabilitation operation in a hospital and remote training center. Prototype development and proof-of-concept demonstrations have occurred for the non-treadmill paddle.



Awards & Recognition

Science and technology advances at a rate that is, in part, related to the number of capable individuals conducting discovery and problem-solving work. The timing of revolutionary breakthroughs may not be predictable, but the chances improve with the number of prepared minds working in the field. This section of the TATRC annual report recognizes eight individuals who each contributed to the collective military medical science and technology effort this year.

TATRC Maxwell Thurman Award

Dr. John Parrish received the Maxwell Thurman Award for his work in the use of advanced technologies to improve patient care.

The Award honors the late Gen. Maxwell Reid Thurman, who championed the advancement of lifesaving medical technologies within the US Army.

Presented by COL Jeff Davies, Chief of Staff, USAMRMC and also by TATRC, the Maxwell Thurman Award is given to a national leader who has made a substantial contribution toward the advancement of telemedicine and related medical technologies in order to improve patient care. It is the Command's top award and is presented each year at the American Telemedicine Association's International Meeting.

COL Jeff Davies presents Dr. John Parrish with the Maxwell Thurman Award.

Dr. Parrish is a nationally recognized innovator, clinician and researcher. His career included tenures as chief of the Massachusetts General Hospital (MGH) Dermatology Service and director of the MGH Cutaneous Biology Research Center. He founded the first, and now the world's largest, multidisciplinary research group to systematically study the nature of laser effects on tissue, The Wellman Center for Photomedicine.

Dr. Parrish founded and leads CIMIT. A center of innovation, CIMIT fosters and nurtures interdisciplinary collaboration among world-class experts in medicine, science and engineering, in concert with industry and government, to rapidly improve patient care. As a non-profit consortium of Boston area teaching hospitals and engineering schools, CIMIT provides innovators with resources to explore, develop and implement novel technological solutions for today's most urgent healthcare problems.

Having served as a battlefield doctor during the Vietnam War, Dr. Parrish is acutely aware of the needs of Warfighters and their supportive medical units. Today, CIMIT is supporting efforts to develop technology that can care for the injured Warfighter in all phases of care, from front lines of the battlefield, through evacuation, restoration and transitioning home for long term care.

"Collaboration has the power to change medicine," Dr. Parrish said in accepting the award. "It is indeed a special honor to be recognized by [USA]MRMC and TATRC, who have become exceptional partners with CIMIT in advancing innovation on behalf of both Service Members and civilians."

PAST AWARD RECIPIENTS

2009: John A. Parrish, M.D.
2008: James H. "Red" Duke, M.D.
2007: Seong Ki Mun, Ph.D.
2006: Mr. Carl E. Hendricks
2005: Gary R. Gilbert, Ph.D.
2004: S. Ward Casscells, M.D.
2003: MG John S. Parker, M.D.
2002: G. Rufus Sessions, Ph.D.
2001: Mr. Conrad A. Clyburn
2000: Greg T. Mogel, M.D.
1999: COL Ron Poropatich, M.D.
1998: BG Russ Zajtchuk, M.D.
1997: CPT Paul Zimnik, D.O.
1996: COL Fred Goeringer

TATRC G. Rufus Sessions Award for Advances in Military Medical Mobile Technology

In 2008, the United States Army, led by USAMRMC and TATRC initiated a collaborative effort to connect Wounded Warriors to their health care team through their personal cell phones. This project is mCare, and the objective is to provide an effective, secure, HIPAA compliant, bidirectional messaging solution directly from the military healthcare team to the Service Members' personal cell phones.

One unique aspect of mCare is its outreach to a predominantly Reserve and National Guard population that has sustained wounds during deployment and is now having their care monitored by a CBWTU. These CBWTUs are geographically dislocated from the service members, and allows them to receive medical care in their home communities.

Jeanette Rasche, Technical Director of the mCare project, has driven the development of the mCare messaging system with our industry partner (AllOne Mobile) in less than a year. As Technical Director, she developed an extensive technical requirements document that served as the blueprint for the mCare technical platform. She also worked with AllOne to scope out several versions of mCare to support the multiple phases of the project.

Her superb strategic planning for developing the technology platform allowed for the execution of Phase I of mCare where over 100 users at 5 CBWTUs were sent over 9,000 secure messages from May 2009 to December 2009. Without her vision and focus this would have not been possible. Support of the mCare initiative required more than just a well laid plan. She also spearheaded negotiations between all four major cellular service providers to ensure that patients would be able to access mCare on their personal cell phones without additional cost for the application or its usage. Additionally, Jeanette has organized a systematic validation of the first version of the mCare application with all members of the mCare team.

Furthermore, she worked with the entire mCare team to identify the requirements for mCare versions that will allow for expansive features in mCare version 2, which incorporate unique mCare additions such as daily status questionnaires.

Ms. Rasche's expertise breathed life into the status questionnaires by creation of algorithms that visually represented the process for the mCare team. These elements are essential to evaluating the potential of this technology and providing the CBWTU care teams with important indicators of the service member's well being. She continues to identify emerging requirements, as discovered by the mCare team, and has interfaced daily with AllOne Mobile to ensure that these improvements are integrated into the second version.

Finally, with a background as a former Medical Illustrator, she makes all the symbols of mCare clean, impeccably polished and incredibly professional. From the design of the cell phone and web interfaces for mCare to the brochures, posters, presentations and monthly newsletters.

Ms. Jeanette Rasche, the first recipient of the G. Rufus Sessions Award, presents an overview of mCare, the program for which she has been recognized.

Legion of Honor

Dr. Jean-Louis Bélard, Senior Clinical Advisor at TATRC, was named a Knight in the Ordre de la Legion d'Honneur (Order of the Legion of Honor), by decree of the French President, Nicolas Sarkozy. This Order, which was created by Emperor Napoleon in 1802, was originally created to reward only military personnel, but during the 20th century, it opened to civilians as well. Men and women from academia, government and industry, can be received into the Légion for "eminent merit." The Order includes the three ranks of Knight, Officer and Commander. In 2006, the US Army Chief of Staff , General Peter Schoomaker, was awarded the Legion of Honor with the rank of Commander.

After a 20-year career in the French Medical Corps, then-Major Bélard was appointed Defense Medical Attaché with the embassy of France in Washington, DC.

Upon leaving active duty with the rank of Colonel, Dr. Bélard took a Visiting Scientist position with the CDC in 1991. In the Division of Safety Research of the National Institute of Occupational Safety and Health, he was responsible for designing, directing and conducting research in the field of human factors and work physiology. During this same time, he served as adjunct Associate Professor of Environmental Medicine at West Virginia University Medical School, and on the faculty of the Department of Military and Emergency Medicine, USUHS in Bethesda, MD. He was granted permanent residency in the United States in the most selective category, "Alien of Extraordinary Ability," in 1996. He joined TATRC in 2000 as a Senior Scientist. His numerous memberships in international scientific societies and associations, his extra-curricular work activities in church and education show a keen interest for the rapprochement of American and French cultures.

This nomination in the Order of the Legion of Honor shows the recognition and the gratitude of the French government not only for the continuation in the AMEDD of an outstanding scientific career, but even more importantly for never-ending efforts to initiate, nurture and consolidate friendly and fruitful relations between the scientific communities of our two countries.

Left: His Excellency Pierre Vimont, Ambassador of France to the United States, pins the cross of Knight in the Legion of Honor on Dr. J-Louis Bélard's lapel.

Above: Dr. Ward Casscells, Assistant Secretary of Defense for Health Affairs, congratulates the new knight during the reception at the Ambassador's residence.

Flemming Award

Presented with the Arthur S. Flemming award, Dr. Jaques Reifman was selected for this prestigious national award because of his outstanding public services and achievements in applied science, engineering and mathematics, while serving as the director of two cutting-edge research organizations which he created: USAMRMC BIC and the DoD BHSAI for Force Health Protection.

Within his seven years of leadership, Reifman has led his team of scientists to the forefront of computational biology research to help improve Warfighters' health by leveraging bioinformatics and high performance computing technologies. These technologies enable the USAMRMC and other DoD organizations to more rapidly develop diagnostic devices, drugs and vaccines to reduce the occurrence of non-battle injuries and the morbidity and mortality of battlefield casualties.

"In 35 years of serving in the Army or working for the Army, I have seen an awful lot of very dedicated and patriotic people but have never seen anyone who works so hard, and is so thorough, and demands so much from himself as does Dr. Reifman," said Gary R. Gilbert, Ph.D., TATRC's chief of Knowledge and Engineering Group.

The Flemming Awards were established in 1948 in honor of Arthur Flemming's commitment to public service throughout his distinguished career, which spanned seven decades.

Pictured (l-r) are Dr. Gilbert, Dr. Glenn, Dr. Reifman, MAJ General Wheeling, COL Davies, & COL Poropatich.

The award is recognized by the President of the United States, agency heads, and in the private sector, 12 annual winners are selected from all areas of the federal service from among three categories: Applied Science, Engineering and Mathematics; Basic Science; and Managerial or Legal Achievement.

Pictured (l-r) are Dr. Steven Knapp, Dr. Reifman, & Dr. Kathryn Newcomer.

Computerworld Honor

Few can argue that most achievements over the last two decades have been influenced in some way — whether large or small— by technology. More importantly, those achievements wouldn't have been possible without the noble passions of people who forged these significant innovations with technology. Computerworld has honored LCDR Steve Steffensen with a Laureate award for his strong commitment and hard work on the NHIN-CONNECT program.

NHIN-CONNECT will transform the medical community by creating a national open architecture upon which multiple services can be built to promote higher quality of care and reduce costs of healthcare delivery.

NHIN-CONNECT will not only benefit Service Members, but facilitates the exchange of information between disparate healthcare organizations and enables interoperability and collaboration between multiple government and civilian agencies. One of the most important benefits of the NHIN is the collaboration and cooperation that is taking place between the federal government and the private sector healthcare community. NHIN will provide a secure, interoperable infrastructure to allow doctors, hospitals, laboratories, pharmacies, and others involved in supporting health and healthcare to share information. Ultimately, this information will follow the Service Member so that it is available whenever and wherever it is needed for clinical decision making. The Service Member will benefit from a higher quality of medical care.

The Computerworld Honors Laureate award celebrates the contributions of LCDR. Steffensen and others who have made contributions to the betterment of society through exceptional—if not heroic—use of information technology. The Computerworld Honors Program remains dedicated to a singular and ongoing mission: "A Search for New Heroes."

This search identifies, acknowledges and preserves the accomplishments of the men and women, organizations and institutions that are creating the world's ongoing IT revolution.

Left: LCDR Steve Steffensen accepts the Computerworld Honors Laureate award for his contribution to the DoD NHIN initiative. Right: LCDR Steffensen with LtCol Jean Meink, Director of Clinical Informatics at DHSS, following the Computerworld Honors award ceremony.

AMEDD Trans-cranial Doppler Program

Dr. Alex Vo's poster—"AMEDD Trans-cranial Doppler Program"—presented at the 12th Annual Army Force Health Protection conference, August 8th - 21st 2009 in Albuquerque, NM, took first prize in the "clinical" category.

Dr. Vo with his General Officers letter and coin, presented for his poster, "AMEDD Trans-cranial Doppler Program," which took first prize in the Clinical category at the Force Health Protection Conference.

Cadet Internship

Cadet William Guinther of the United States Military Academy (USMA) completed a three-week long internship with the APHP research portfolio at TATRC in July, 2009. In conclusion of his internship, Cadet Guinther presented a prosthetics technology gaps analysis report to Portfolio and TATRC leadership. Guinther's program consisted of studying both the research program overseen by TATRC and the clinical procedures of WRAMC. By combining these two experiences, Cadet Guinther was able to analyze the current state of research and offer suggestions as to where future research may be guided. Cadet Guinther was hosted by Ashley Fisher, Adam Kisielewski, and Troy Turner of TATRC's APHP portfolio.

In addition to TATRC's APHP portfolio, Guinther's work also benefits the "West Point Bionic Foot (WPBF)" TATRC funded research project at the USMA, managed by LTC Joseph Hitt, Ph.D. Under the supervision of LTC Hitt, the WPBF project seeks to develop a powered ankle to better meet the needs of our amputee Warfighters.

Guinther's internship and performance has paved the way for future Cadet interns to also serve at TATRC, contributing to the advances that help us care for our military family.

Cadet William Guinther, as part of an internship through the USMA, was able to analyze the current state of research and offer suggestions as to where future research may be guided.

Engineer and Scientist Exchange Program (ESEP)

The Engineer and Scientist Exchange Program (ESEP) is a professional development program that promotes international cooperation in military research, development, test and evaluation (RDT&E) through the exchange of military and/or government civilian engineers and scientists. ESEP provides on-site working assignments for foreign personnel in US defense establishments, and for US personnel in foreign defense establishments. The work assignments shall provide ESEP personnel work experience and knowledge of the organization and management of that defense establishment by performing duties of the assigned Position Description under the direction of a host supervisor. ESEP assignments take place under a valid master bilateral MOU. The ESEP program leverages state-of-the-art technology of mutual interest to the US and the foreign country involved and conserves scarce resources by reducing duplicative RDT&E efforts. Participation in ESEP is on a highly selective basis from among career military and government civilian personnel of the US Army and participating foreign defense activities. The selectees must have demonstrated capabilities for future positions of greater responsibility; be well versed in current practices, technical training and doctrine of their organization; and be particularly qualified through experience for the positions to be occupied.

Mr. Marco Konzer, German Military Liaison Officer, assigned to TATRC from July 2009 through June 2010, key member of the CDE Team.

Mr. Marco Konzer arrived at TATRC on July 3rd, 2009 and is assigned to the Advanced Information technology Group. His experience in project management, especially in contract negotiation and management, as well as directing various software development projects helped him to quickly adjust to his new assignment at TATRC.

PAWS, a software product developed within TATRC, is in the process of being going into production with AHLTA. PAWS extracts up to 12 data domains from AHLTA making the data available to secondary clinical systems outside of AHLTA. PAWS is crucial part of the DoD's link with the NHIN/VLER. Mr. Konzer contributed to the release of PAWS by assisting in documentation standards, repeatedly reviewing and assembling the documentation set for PAWS, and assisting in the coordination of its delivery to the DHIMS Program Office and other major stakeholders.

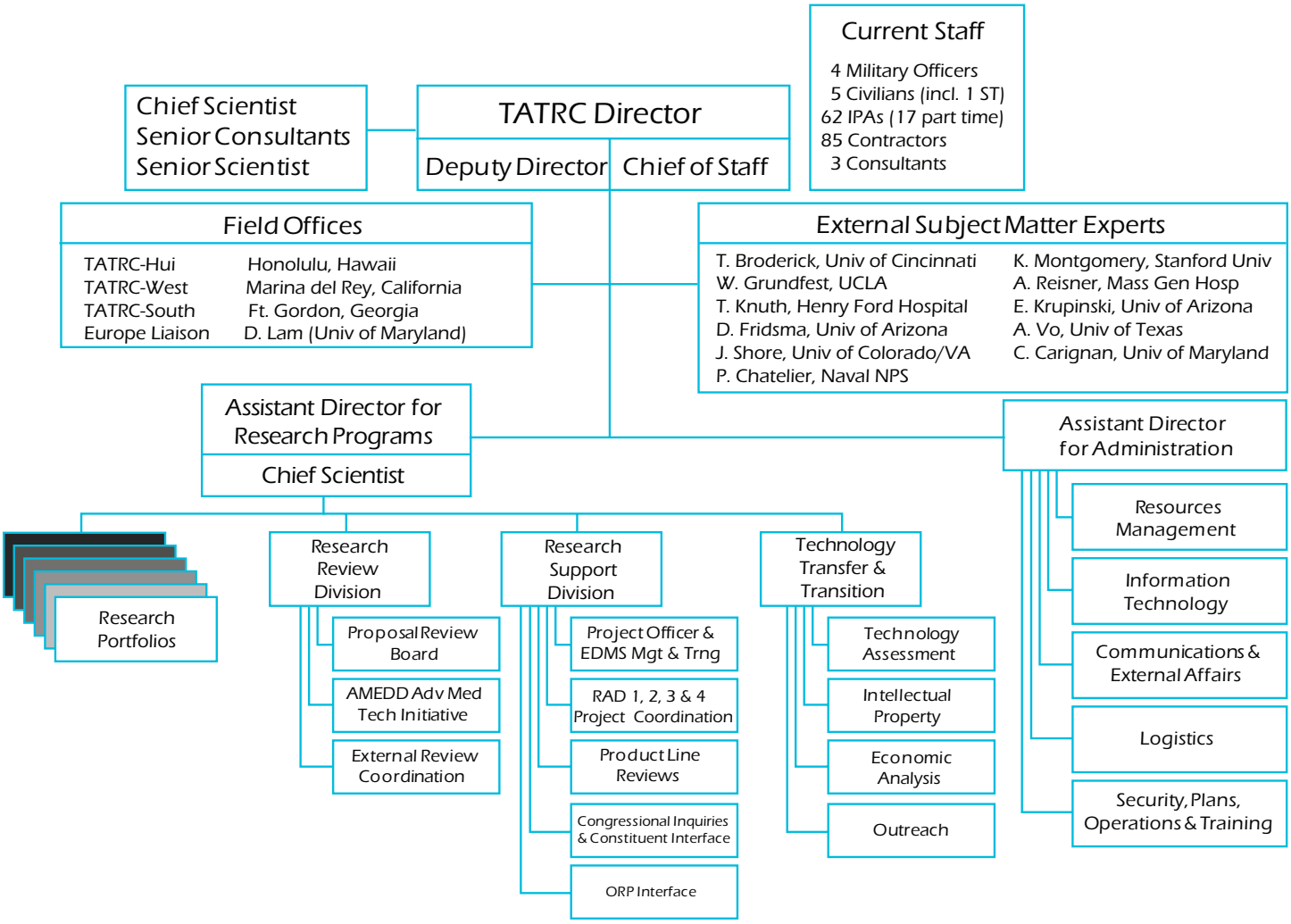
Furthermore, Mr. Konzer executed qualitative tests especially of PAWS modules; reviewing and writing a set of queries to extract test data sets.

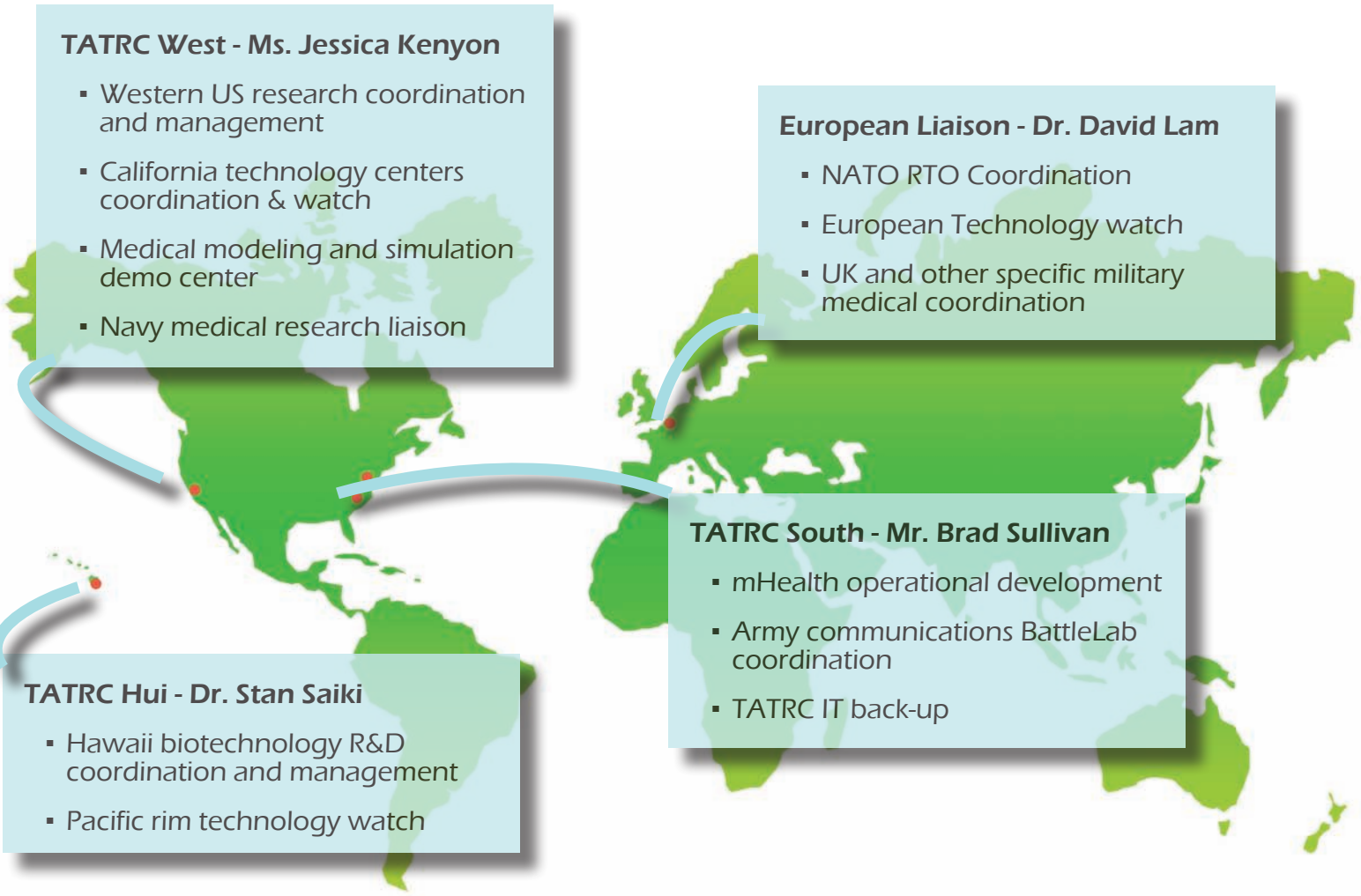
Mr. Konzer is currently working with the CDE Projects Manager, Mr. Mark Jeffrey, as they work on two key projects that will affect the AHLTA enterprise: AHLTA Print and the AHLTA/Essentris Project. AHLTA Print will provide users the ability to print out complete or partial patient medical records from AHLTA either in a single request or batch mode; the Essentris Project takes the in-patient Essentris System's Patient Emergency Department Summary Record and write it into the out-patient AHLTA system which will provide a more complete patient health record and enable the MHS to recover lost Relative Value Unit credits.

Mr. Konzer works closely with the AITG CDE Team where he has contributed in the expansion of the CDE as it meets the research and development, as well as, operational needs of the MHS.

Organization and Capabilities

TATRC is organized to maximize the return on investment from taxpayer funds, with transitions to core or advanced programs or directly to military implementation. The focus is on research portfolios that represent interrelated and cross cutting technologies and sciences to address key military medical gaps. TATRC also provides direct assistance in the development of capabilities in research regulatory compliance issues, connecting with military customers, and transitioning products to implementation. Slightly more than 150 individuals directly support the TATRC mission.





European Office

Brussels, Belgium

Though it is small and served by only one individual, David Lam, M.D., MPH, COL (ret.), the TATRC European Office remains a unique asset for the organization, being the only TATRC asset permanently located outside of the United States.

In the 2001 Army Science and Technology Master Plan, cooperative science was recognized as a strategic tool; global technology and research was strongly emphasized among our allies in NATO.

The major focus of this office is in the operational telemedicine area, and it also provided the Secretary/Assistant Chairman for the NATO Telemedicine Expert Panel. This panel has been most successful in migrating telemedicine capabilities and technologies into the NATO environment, and in developing and having promulgated a NATO Standardization Agreement (STANAG 2517) to assist nations in the development of Teleconsultation efforts. TATRC continues to provide the benefits of our developed expertise in support of NATO efforts to develop doctrine and policy for the interoperable use of telemedicine and other advanced medical technologies in a multinational deployed environment. The recent development and fielding of a MOU authorizing NATO forces in Afghanistan to make use of the deployed AKO Teleconsultation system is a direct outcome of these efforts.

An increased number of Research and Technology Organization Technology Teams have been formed which directly address topics of interest to the USAMRMC and TATRC core competencies.

The office has provided representation to other NATO working groups, including the Medical Standardization Working Group and the Medical Communications and Information Systems Expert Panel. Intermittent support has been provided to other groups on both the Civil and Military sides of NATO, including the Joint Medical Committee, the Civil Communication Planning Committee, and the Science For Peace Program. The mission has been extended to maintaining cognizance of the relevant research programs of the European Commission, the European Research Area, the European Space Agency, and World Health Organization.

TATRC South

TATRC South Field Office
Fort Gordon, Georgia

The TATRC South field office in Augusta, GA, is a tenant activity within the SERMC campus.

Ft. Gordon is the home of the US Army Signal Corps, which provides and manages communications and network operations for the combined tactical forces, to include supporting medical units within the operational environment.

TATRC has partnered with a subcomponent of the Signal Corps, the Experimental Division, Battle Command Battle Laboratory-Gordon (BCBL-G). This unique organization is a member of the Federated Battle Laboratory consortium, and is chartered as a research, analysis, prototyping, experimentation and test facility. This mission supports future tactical requirements, including medical operations. TATRC's partnership is leveraged to conduct experimentation and evaluation of technologies resulting from Congressional Special Interest projects, to include special projects internal to MEDCOM.

The TATRC South field office is centered in one of the most densely populated areas of deployable military assets. Including Ft. Benning, Ft. Stewart, Ft. Campbell and Ft. Bragg.

The Medical College of Georgia (MCG) is the state's only public academic medical campus. Two of the current TATRC South staff maintain adjunct faculty credentials with this institution, and serve as liaisons to the subject matter expertise that this facility affords to TATRC projects. Most recently this relationship has resulted in a new partnership with the MCG Department of Biostatistics, where data analysis for one of the special interest projects (mCare) will be conducted.

TATRC South has partnered with the Central Savannah River Area (CSRA) Wounded Warrior Care Project, a local non-profit organization, to form the CSRA Medical Research Consortium. This assembly includes key staff members from the Charlie Norwood VA Medical Center, Savannah River National Laboratory, Dwight David Eisenhower Army Medical Center, and the MCG.

TATRC South houses redundant hardware and backups of critical information technology functions, to ensure continuity for key information systems is maintained.

Another component of the TBI special project effort is mCare, a cell phone based outreach

program which is highlighted separately in this edition of the TATRC Annual report. The mCare core team, including Project Management, dedicated IT support and primary infrastructure is administered from the TATRC South field office.

A long-standing relationship with the US Special Operations Command (USSOCOM) Surgeon's office has resulted in TATRC South's collaboration for both the first and second edition of the Special Operations Forces (SOF) Medical Handbook. TATRC South is serving in an advisory capacity to develop the electronic version and is working with the USSOCOM Surgeon to package this material for mobile devices in order to allow the SOF medic to be well prepared to render humanitarian aid in an operational environment.

TATRC West

TATRC West Coast Field Office
Marina del Rey, California

TATRC West was established to strengthen ties with research partners in the western half of the United States and to build collaborative relationships that advance medical technology in support of the Warfighter. It is uniquely positioned to utilize resources that, as yet, remain largely untapped by the military medical community. TATRC West fills a niche that complements the organization as a whole. Simultaneously, its staff of scientists and other personnel play a critical role in the project oversight mission of the enterprise across a range of scientific domains.

Since its founding in 2005, TATRC West has demonstrated success in building strong relationships with academic research partners, such as the CASIT at UCLA, the University of Southern California ICT, the UC system-wide Institute for Engineering in Medicine, and NCIRE. The West Coast office has also formed strong ties with other DoD organizations in the region, such as the NHRC, the NMCSD, and others. TATRC West has also made inroads into the commercial world, developing ties with such organizations as Qualcomm, RAND Corporation, the Southern California Biomedical Council (SCBC), and the Larta Institute, among others.

TATRC West is located blocks away from the ICT, an Army-funded University-Affiliated Research Center (UARC). At the ICT, TATRC has funded multiple projects on medical virtual reality applications, such as PTSD treatment and "SimCoach," a virtual human computer interface for Service Member assistance.

The Samueli Institute's West Coast office and RAND are also close neighbors of TATRC West. Samueli, has partnered with RAND to develop the evaluation methodologies currently in use for the WAROPS Program at Fort Carson, CO. WAROPS is a training program designed to help Warfighters manage operational stress while maximizing performance and combat readiness.

TATRC West maintains close connections with NHRC in San Diego to ensure that this Navy lab is part of USAMRMC's and TATRC's project collaborations and management.

Several TATRC portfolio managers reside in the western region, and are headquartered at the TATRC West office. Portfolios represented are Biomaterials and Nano-medicine, Behavioral Health, Disaster Medicine, and Acoustic Trauma.

TATRC West's geography also affords it other unique opportunities. It is working to become known in the investment community through venture capital groups, etc. As potential investors and industry partners begin to view TATRC as a pipeline for emerging technology, TATRC's research products stand a greater

chance of successful transition to the marketplace or to military users.

TATRC West also aims to foster increased interest in military-relevant medical research among the scientific community in the western United States and the Pacific Rim by engaging in large, national scientific meetings such as those put forth by SPIE, the American Institute for Medical and Biological Engineering (AIMBE), and the Diabetes Technology Society.

TATRC West is currently at work on establishing a center for the showcasing and demonstration of simulation and training technology in an effort to facilitate technology transfer and to broaden collaborations across civilian and military partners in that domain. The office's close proximity to many key partners in the simulation community make it uniquely suited to take on this task.

TATRC Hui, Pacific Telehealth & Technology Hui

Honolulu, Hawaii

In December 1999, a MOU was executed between TAMC and Spark M. Matsunaga Veteran Affairs Medical Center (VAMC Honolulu) to create a partnership now known as the Pacific Telehealth & Technology Hui. The Hui was established with congressional funding to leverage mutual strengths and improve the quality, accessibility, patient satisfaction, and cost-effectiveness of healthcare services provided to beneficiaries through the use of emerging technologies and telehealth technologies involving research, development, prototype, evaluation and technology transfer.

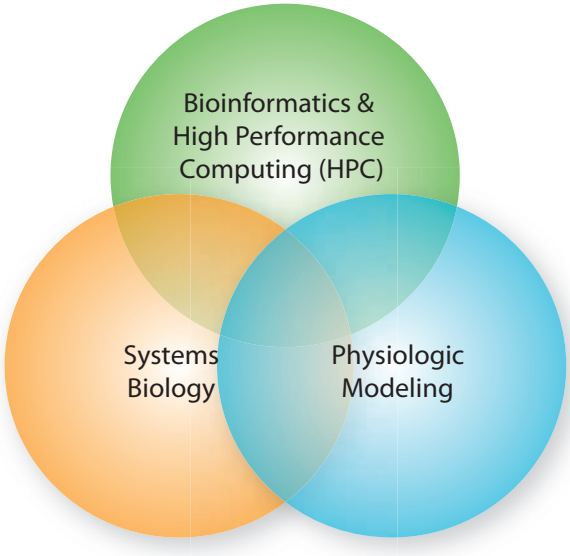
Hui collaboration with public and private sector customers and stake-holders fosters successful prototyping, demonstrating, and validating of new healthcare technologies to raise the quality, accessibility, patient satisfaction, and cost-effectiveness of healthcare services.

As a field office of TATRC, the Hui supports applied research and the development and deployment of telehealth and healthcare technology to improve access and the quality of care to military families, federal beneficiaries, and impacted communities. In 2009, the Hui oversaw a portfolio of approximately 30 projects totalling more than $20M.

The DoD Biotechnology High Performance Computing Software Applications Institute (BHSAI)

Frederick, Maryland

The DoD Biotechnology High Performance Computing Software Applications Institute (BHSAI) was established within USAMRMC to meet the Department's needs for in-house expertise in Computational Biology. The BHSAI is led by a senior scientist, Dr. Jaques Reifman, and consists of a cadre of more than 25 Ph.D.-level physical scientists, who serve as an inter-disciplinary resource to accelerate research and development of militarily relevant medical products for Force Health Protection. The Computational Biology research at the BHSAI cuts across the Command's and DoD's missions, ranging from artificial intelligence algorithms for the development of automated decision-aid algorithms to bioinformatics tools to support the design of diagnostic assays to systems biology research to help identify drug and vaccine candidates.

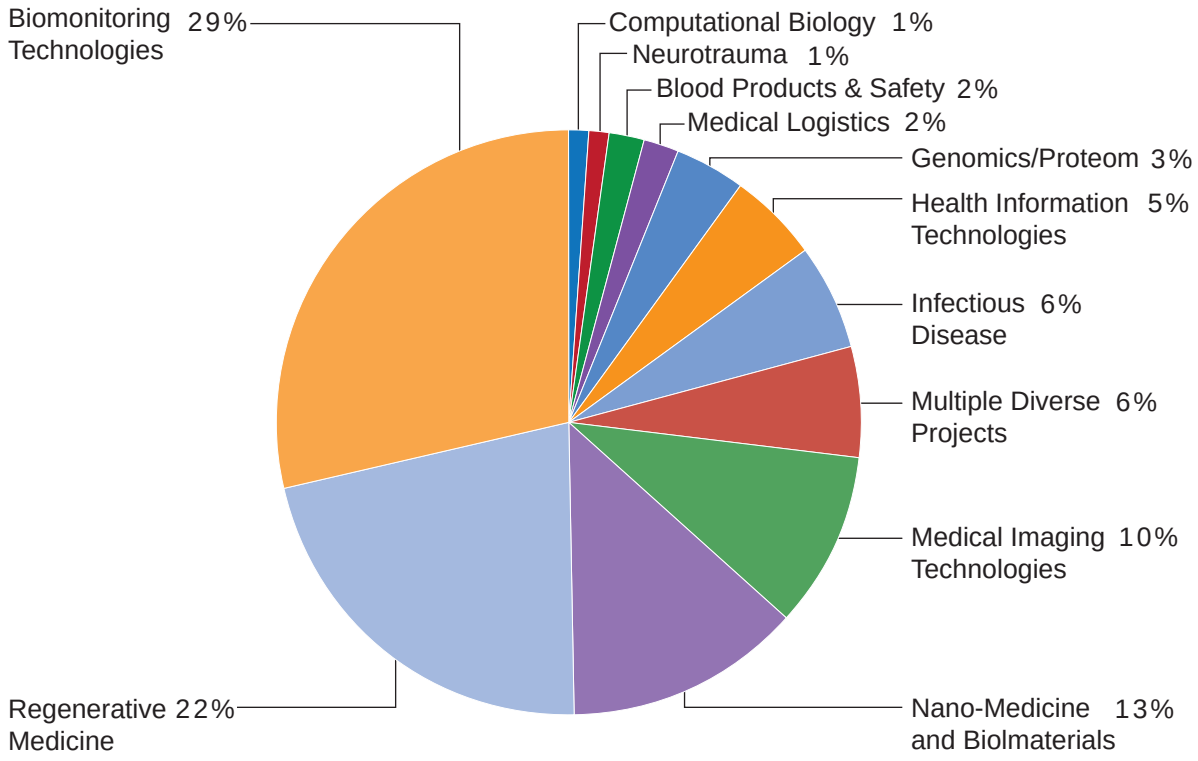


The BHSAI is involved in three interrelated areas of computational biology, that are of special importance to advancing DoD medical research.

Technology Transfer & Transition

TATRC is the USAMRMC's Federal Laboratory Consortium member dedicated to investing and managing extramural seed and early stage advanced medical technology research and development. Its diverse assortment of unique collaborative relationships with government, academia, and industry under the Bayh-Dole Act of 1980 (P.L. 96-517) together with Patent and Trademark Clarification Act of 1984 (P.L. 98-620) "provides small businesses, universities, and not-for-profit organizations opportunities to obtain titles to inventions developed with federal funds" (Federal Technology Transfer Legislation and Policy, 2005, p.vii). Through collaboration with the Office of Technology Transfer (OTT), Undersecretary of Defense, Acquisition Technology and Logistics, TATRC is targeting specific technologies for commercialization with expert Partnership Intermediaries sponsored by the OTT.

As TATRC mines its technology transfer/transition data to determine its affect in catalyzing technology commercialization from this public and private collaboration, the initial results are significant. Intellectual Property data (e.g., Patent Application and Patent Approval) is being aggressively pursued. Thus far, over 300 patents have been identified as filed by TATRC partners. The long term goal is to measure economic effect (e.g., Licenses, Acquisition, Jobs created, and Taxes generated) of federally funded R&D through the TATRC Program.



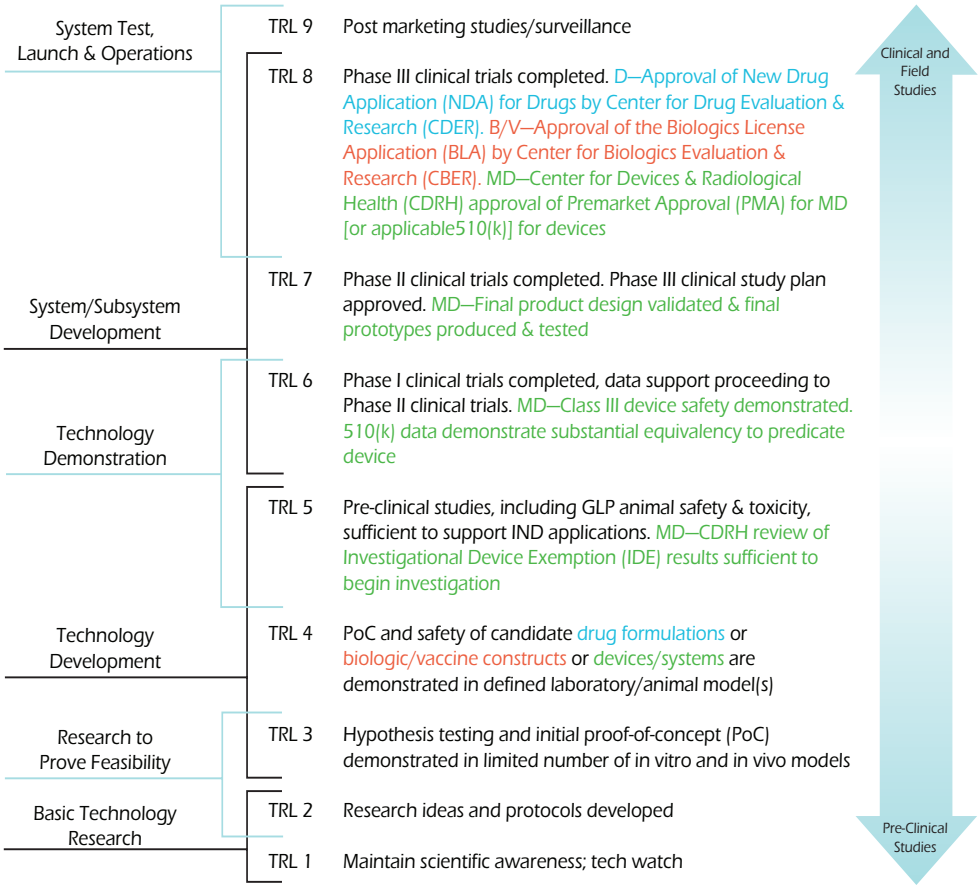
Patents Filed by Research

Drug and Biological Development Phases
Pre-Clinical and Clinical Trial Definitions

Phase	Population	~ Number of Subjects Required	Purpose
Pre-clinical	Highly controlled (GLP) studies in animals	Hundreds to Thousands	Safety, toxicity, effectiveness. Provides evidence to FDA safe enough to try in humans
I	Healthy volunteers Exception: Cancer/ AIDS etc.	20 to 80 subjects/trial	Safety
II	Subjects with the Illness (narrow population)	24 to 300 subjects/trial	Safety Effectiveness Dose
III	Subjects with the Illness (broad population)	250 to 3000 subjects/trial	Confirming safe and effective in diverse populations
IV/V	Subjects with the Illness; Special population (very broad population)	FDA and Sponsor negotiate	After FDA approval (Post-licensure), for safety and/or other uses

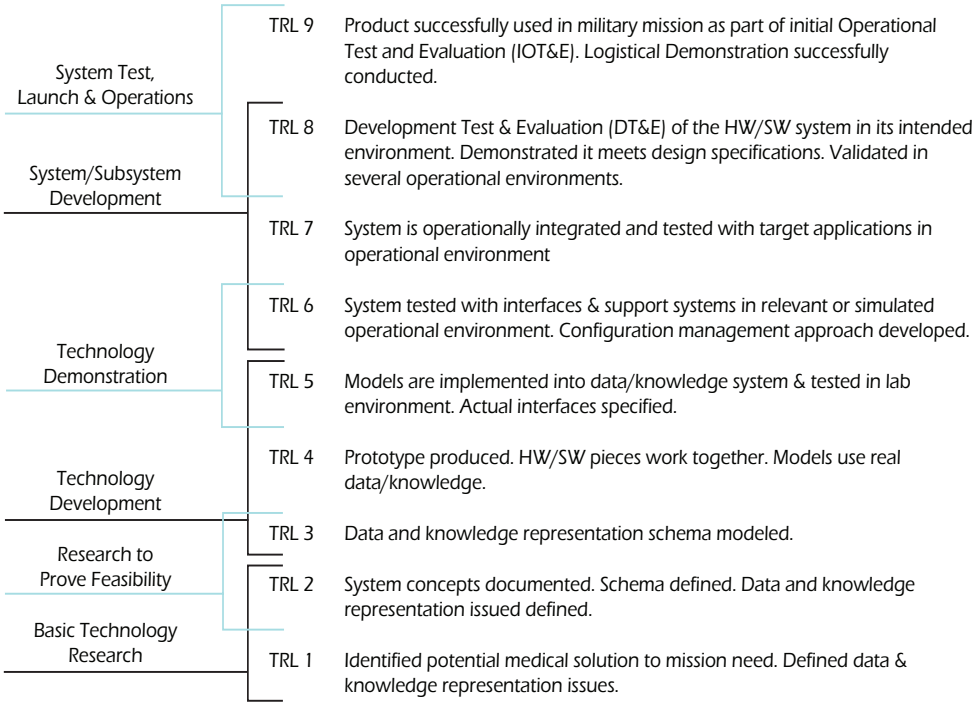
Biomedical Technology Readiness Levels

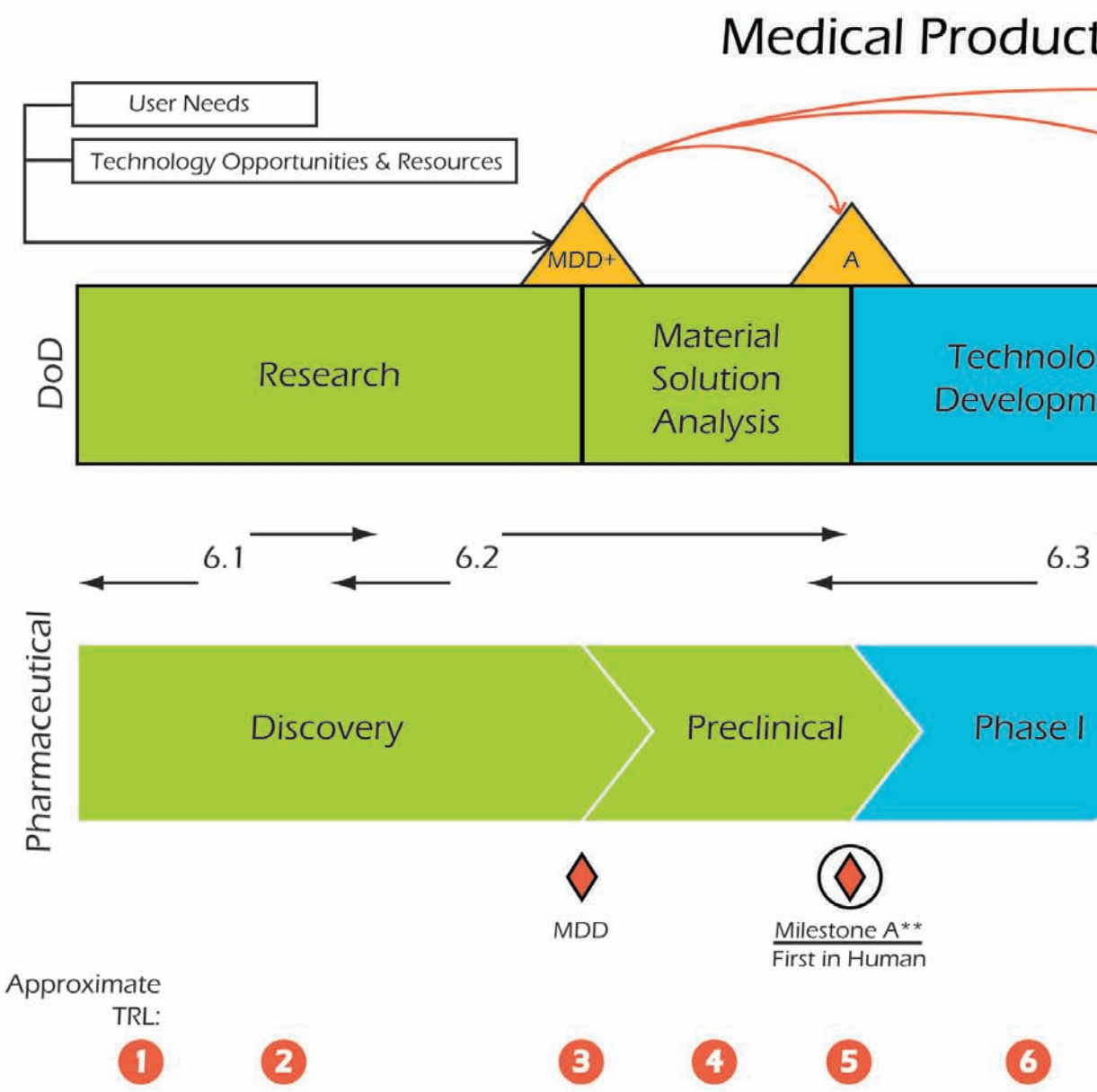
D—Pharmaceutical (Drugs); B/V—Pharmaceutical (Biologics, Vaccines); MD—Medical Devices; Same for All



Biomedical Technology Readiness Levels

Medical IM/IT & Medical Informatics





* Based on agreed development plan and back-up strategy multiple candida

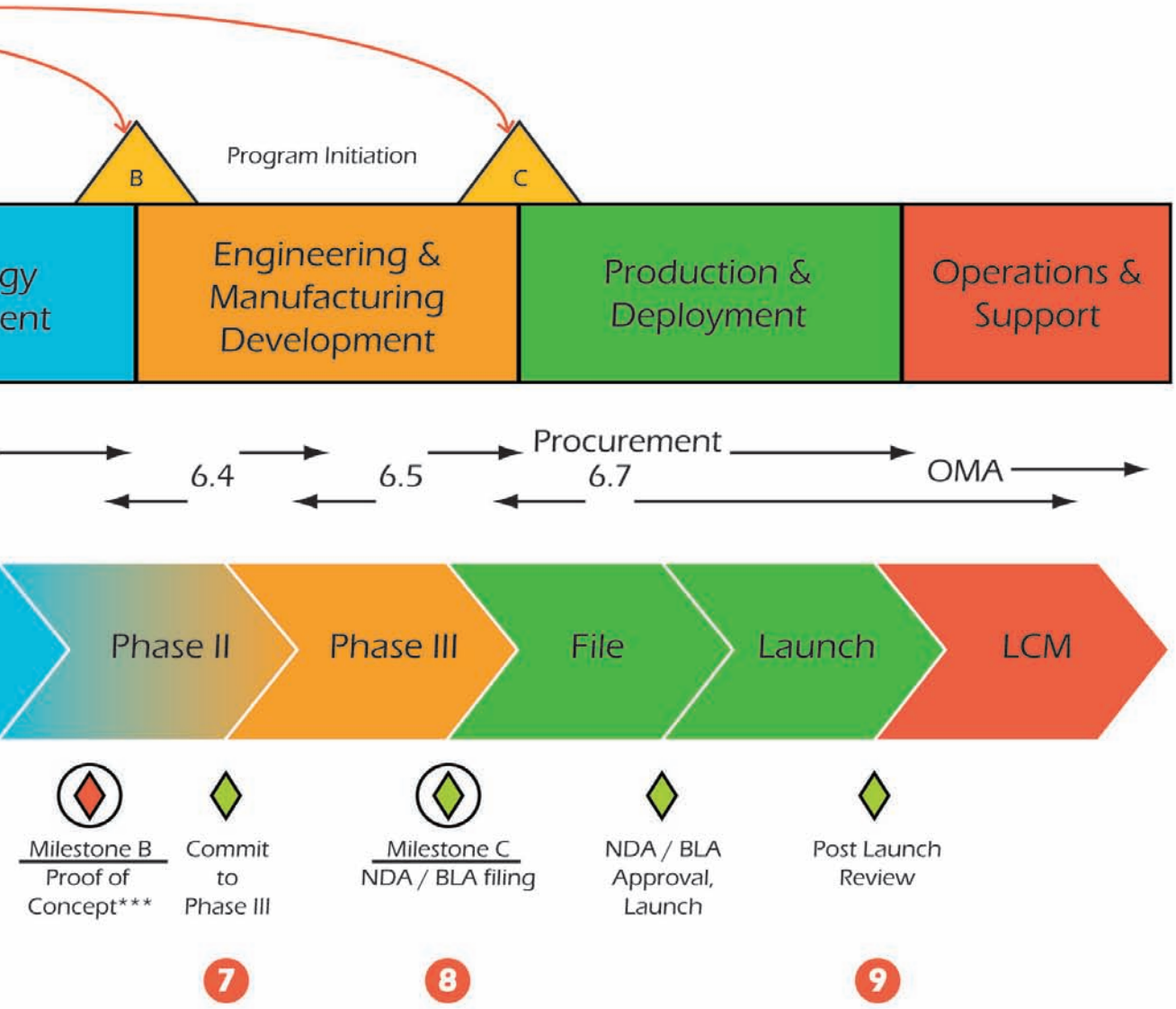
** First in human (FIH) decision should occur after meeting the FDA pre-Inve projects will have a pre-IND meeting.

** If FIH is a small trial, a Milestone A may occur after positive results are obtai situation, a FIH meeting with the CG will still be required.

*** Proof of concept occurs when evidence of safety and efficacy provide suf and IIb but varies by product.

+ Mandatory Materiel Development Decision (MDD) precedes entry into any p

t Development Lifecycle



tes may move through the development process.

stigational New Drug Application (IND) meeting if being conducted. Not all

ned to understand if there is a potential materiel solution to a known threat. In this

fficient confidence to invest in larger studies. This typically falls between Phase IIa

hase of the acquisition system.

Acronyms and Definitions

A

AAMTI	AMEDD Advanced Medical Technology Initiative
AMEDD	Army Medical Department
ABRT	activity-based restorative therapy
ABS	active beam scanning
ACR	American College of Radiology
ADR	Adverse drug reactions
AFCHIPS	Air Force Corporate Health Information Processing Service
AFHSC	Armed Forces Health Surveillance Center
AFIRM	Armed Forces Institute of Regenerative Medicine
AFPT	Army Physical Fitness Test
AGS	Arctic Ground Squirrel
AHLTA	Armed Forces Health Longitudinal Technology Application
AIMBE	American Institute for Medical and Biological Engineering
AK	above the knee
AKI	acute kidney injury
AKO	Army Knowledge Online
AMPS	Alternative Mobile Power Station
ANAM	Automated Neurological Assessment Metrics
ANH	Alliance for NanoHealth
ANT	Ad hoc Networked Tags
AOR	Area of Responsibility
APHP	Advanced Prosthetics and Human Performance
ARL	Army Research Lab
ARRA	American Recovery and Reinvestment Act
ARVO	Association for Research in Vision and Ophthalmology
ASC	Adipose-derived stromal cells
ASC	Accelerated Screening Cascade
ATACCC	Advanced Technology for Combat Casualty Care
ATF	Athletic Trainer-Forward

B

BAACH	Brian Allgood Army Community Hospital
BCBL-G	Battle Command Battle Laboratory Gordon
BCT	basic combat training
BEAR	Battlefield Extraction Assist Robot
BHIE	Bi-Directional Health Information Exchange
BHSAI	Biotechnology High Performance Computing Software Application Institute
BIC	Bioinformatics Cell
BIOWARS	Biosurveillance-based Integrated Outbreak Warning And Recognition System
BK	below the knee
BLE	Blended Learning Ecologies
BoNT/A	Botulinum neurotoxin serotype
BPEI	Bascom Palmer Eye Institute
BTA	biological threat agent
BWH	Brigham and Women's Hospital

C

CAL	Common Access Layer
CAM	complementary and alternative medicine
CAPS	Clinician-Administered PTSD Scale
CAREN	Computer Aided Rehabilitation Environment
CASEVAC	casualty evacuation
CASIT	Center for Advanced Surgical and Interventional Technology
CAVE	Computer Aided Virtual Environment
CBCP	Clinical Breast Care Project
CBI	classroom based instruction
CBI	Cellular Bioengineering, Inc.
CBRNE	chemical, biological, radiological, nuclear, and high yield explosives
CBWTU	Community Based Warrior in Transition Unit
CCCRP	Combat Casualty Care Research Program
CCD	Continuity of Care Documents
CCR	Continuity of Care Records
CDA	Clinical Document Architecture
CDC	Centers for Disease Control and Prevention
CDE	Clinical Development Environment
CDHAM	Center for Disaster and Humanitarian Assistance Medicine
CDR	Central Data Repository
CERMUSA	Center of Excellence for Remote and Medically Underserved Areas
CHAMP	Comprehensive High-level Activity Mobility Predictor

CHCS	Composite Health Care system
CIM	Center for International Medicine
CIMIT	Center for Integration of Medicine and Innovative Technology
CIND	Center for Imaging of Neurodegenerative Diseases
CLS	Combat Lifesaver
CME	Continuing Medical Education
CMU	Carnegie Mellon University
CNNP	Comprehensive National Neuroscience Program
COCOM	Combatant Command
COMEDS	Chiefs of the Military Medical Services
COMETS	Combat Medic Training System
COTS	commercial off-the-shelf
CPOE	Computerized Physician Order Entry
CPP	Commercialization Pilot Program
CR	computed radiography
CRF	case report form
CRIMM	Center For Research On Integrative Medicine
CRMRP	Clinical and Rehabilitative Medicine Research Program
CRS	clinical reporting system
CSH	combat support hospital
C-SHOP	Center for the Study of Human Operator Performance
CSRA	Central Savannah River Area
CT	computed tomography
CTEC	clinical treatment and evaluation centers

D

DAI	Diffuse Axonal Injury
DARPA	Defense Advanced Research Projects Agency
DBS	deep brain stimulation
DCoE	Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury
DEERS	Defense Enrollment Eligibility Reporting System
DHIMS	Defense Health Information Management System
DHSS	Defense Health Services System
DIACAP	DoD Information Assurance Certification and Accreditation Process
DISA	Defense Information Systems Agency
DL	direct laryngoscopy
DMZ	demilitarized zone
DNS	dietary and nutritional supplement
DoD	Department of Defense
DOVIS	Docking-based Virtual Screening
DR	digital radiography
DRC	Democratic Republic of the Congo
DMRTI	Defense Medical Readiness Training Institute
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSO	Defense Science Office
DT&E	development test and evaluation
DTI	Diffusion Tensor Imaging
DTI	Diffusion Tensor imaging
DVBIC	Defense and Veterans Brain Injury Center
DVEIR	Defense and Veterans Eye Injury Registry

E

EAE	Experimentation and Analysis Element
EBT	External beam therapy
ECG	electrocardiogram
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
EEG	electroencephalogram
EHR	Electronic Health Record
EMI	ElectroSonics Medical, Inc
EPA	Environmental Protection Agency
EPC	endothelial progenitor cells
ESEP	Engineer and Scientist Exchange Program
EST	expressed sequences tag
ETAP	Evaluation Technical Assistance Project

F

FANTI	FDA-ANH Nanotechnology Initiative
FDA	Food and Drug Administration
FES	functional electrical stimulation
FHA	Federal Healthcare Architecture
FHP&R	Force Health Protection & Readiness
FIMT	Federal Interagency Management Team
FST	Forward Surgical Hospital

G

GCC	Gynecologic Cancer Center
GEIS	Global Emerging Infections Surveillance and Response System
GHz	Gigahertz
GIS	geographic information system
GLP	good laboratory practices
GME	graduate medical education
GPS	Global Positioning System
GUARDIAN	Geographic Utilization of Artificial Intelligence in Real-Time for Disease Identification and Notification

H

H.E.A.L.T.H	Healthy Eating, Activity, Lifestyle Training Headquarters
HAI	Hospital-acquired infections
HBI	Hawaii Biotech, Inc.
HEA	Human Erythrocyte Antigen
Health ICT	Health information and communications technology
HERL	Human Engineering Research Laboratories
HFHCN	Hawaii Federal Health Care Network
HFPA	Health Facilities Planning Agency
HHS	US Department of Health and Human Services
HIFU	High Intensity Focused Ultrasound
HIT	Health Information Technologies
HITSP	Healthcare Information Technology Standards Panel
HOF	Hospital of the Future
HOSTS	Haptics-Optional Surgical Training System
HPC	High Performance Computing
HPE	Human Performance Enhancement
HPO	Human Performance Optimization
HS	hemorrhagic shock

I

ICT	Institute of Creative Technology
ICU	Intensive Care Unit
IED	improvised explosive devices
IETF	Internet Engineering Task Force
IH	integrative health
IHD	International Health Division
IHS	Indian Health Service
IMT	Initial Military Training
IPAM	Institute for Pure and Applied Mathematics
IPEHD	Institute for Partnerships to Eliminate Health Disparities
ISIS	Imaging Science and Information Systems
IVeH	International Virtual e-Hospital Foundation

J

JAUS	Joint Architecture for Unmanned Systems
JCTD	Joint Capability Technology Demonstration
JHU APL	Johns Hopkins University Applied Physics Laboratory
JIF	Joint Incentive Funds
JMDSE	Joint Medical Distance Support and Evacuation
JPL	Jet Propulsion Laboratory
JTCG	Joint Technical Coordinating Group

K

KIM-1	kidney injury molecule-1
KWCMC	Kapiolani Women's and Children's Medical Center

L

LE	lower extremity
LEAPPS	Liner and Electroactive Oplymer Prosthetic Socket
LIBS	Laser Induced Spectrometry
LSTAT	Life Support for Trauma and Transport

M

MAIRP	Military Amputee Intramural Research Program
MAPCP	Military Amputee Patient Care Program
MARP	Military Amputee Research Program
MCG	Medical College of Georgia
MCMI	Miami Center for Ophthalmic Innovation
MDR	Medical Data Repository
MDU	Medication Delivery Unit
MEMS	Micro-Electro-Mechanical Systems
METTA	Military Eye Trauma Treatment Act
MGH	Brigham and Women's Hospital
MGH	Massachusetts General Hospital
MHS	Military Health System
MIR	Micropower Impulse Radar

MOLLE	Modular Lightweight Load-carrying Equipment
MOMRP	Military Operational Medicine Research Program
MOU	Memorandum of Understanding
MPC	esenchymal stem/progenitor cells
MRI	Magnetic resonance imaging
MRS	MR Spectroscopy
MRSA	Methicillin-resistant Staphylococcus Aureus
MSO	Medical Stability Operations
mTBI	mild traumatic brain injury
MUSC	Medical University of South Carolina

N

NAEVR	National Alliance for Eye and Vision Research
NARMC	North Atlantic Regional Medical Command
NASA	National Aeronautics and Space Administration
NATO HFM	North Atlantic Treaty Organization Human Factors & Medicine
NCAT	Neurocognitive Assessment Test
NCCAM	National Center for Complimentary and Alternative Medicine
NCE	Neuroscience Center of Excellence
NCI	National Cancer Institute
NCIRE	Northern California Institute for Research and Education
NEER	National Eye Evaluation Research
NEMB	NanoEngineering for Medicine and Biology
NETPR	Neurotoxin Exposure Treatment Parkinson's Research Program
NFGC	National Functional Genomics Center
NGO	nongovernmental organizations
NHIN	National Health Information Network
NHRC	Naval Health Research Center
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke
NIR	Near-Infrared
NIRS	Near Infrared Spectroscopy
NMCSD	Naval Medical Center, San Diego
NMRC-D	Naval Medical Research Center Detachment
NNMC	National Naval Medical Center
NPA	National Partnership for Action
NRH	National Rehabilitation Hospital
NSF	National Science Foundation
NSTL	National Software Testing Labs

O

OATH	Initiative for Open Authentication
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
ONE SAF	One Semi-Autonomous Forces
ONOVA	Ophthalmic Innovation
ONR	Office of Naval Research
OSD	Office of the Secretary of Defense
OTSG	Office of the Surgeon General
OTT	Office of Technology Transfer

P

PACS	picture archiving and communication systems
PAWS	Patient Ancillary Web Services
PBT	Proton Beam Therapy
PCR	polymerase chain reaction
PCR-RFLP	PCR–Restriction Fragment Length Polymorphism
PD	Parkinson's Disease
PDT	photodynamic therapy
PDTS	Pharmacy data transaction system
PEM	Proton Exchange Membrane
PET	Positron emission tomography
PHAD	Portable Hazardous Agent Detection
PHI	personal heath information
PII	Personal Identifiable Information
PIPA	Pipeline for Protein Annotation
PLR	Product Line Reviews
POM	program objective memorandum
PPP	public-private partnership
pQCT	peripheral Quantitative Computed Tomography
PRAC	Percutaneous Respiratory Assist Catheter
PRAL	Paracorporeal Respiratory Assist Lung
PRT	Pathogen Reduction Technology
PSPP	Protein Structure Prediction Pipeline
PT	Physical Training
PTSD	post-traumatic stress disorder
PVC	Pharmacovigilance Center

R

R&D	research and development
RAD	Research Area Directorate
RAIDER	Rapid Adverse Identifier for Drugs and Evaluation Resource
RDT&E	research, development, test & evaluation
REC	Regional Extension Center
REV	Robotic Evacuation Vehicle
REX	Robotic Extraction Vehicle
RFID	radio frequency identification
RMC	Regional Medical Center
RMLS	Rugged Mobile Logistics System
ROBI	Robotic Bio Identification
RONA	Robotic Nursing Assistant
RRC	Regional Readiness Command
RRT	rapid response team
RSC	Respiratory Support Center
RSS	rich site summary
RT	remote technologies

S

SA	situational awareness
SAIC	Science Applications International Corporation
SAN	squad-area-network
SASP	Self-Actuating Signal Producing
SBIR	Small Business Innovation Research
SDE	Software Development Environment
SERI	Schepens Eye Research Institute
SERMC	Southeastern Regional Medical Command
SFVAMC	San Francisco VA Medical Center
SHI	Strategic Health Intelligence, LLC
SHPERHD	Soldier Health Promotion to Examine and Reduce Health Disparities
SOS	sensor on a strip
SOSTS	Simulation-Based Open Surgery Training System
SPAA	Steerable Phased Array Antenna
SPARNET	Spartan network
SPECT	Single photon emission computed tomography
SPIO	Superparamagnetic iron oxide
SSL	secure socket layer
STTR	Small Business Technology Transfer Program

T

TAMC	Tripler Army Medical Center
TAMIS	Telerobotics and Advanced Minimally Invasive Surgery
TATRC	Telemedicine and Advanced Technology Research Center
TBI	Traumatic Brain Injury
TCD	Transcranial Doppler
TCIA	target controlled infusion anesthesia
TGI	Tissue Genesis, Inc.
THIE	TRICARE Health Information Exchange
THz	Terahertz
TLS	transport layer security
TMR	targeted muscle reinnervation
TOFI	Tool for Oligonucleotide Fingerprint Identification
TRAP	Translating Ribosome Affinity Purification
TRIM	Troop Recruitment Improvement
TRMDU	TelePharmacy Robotic Medication Delivery Unit
TTA	transtibial amputation
TTI	torso-tactile interface
TUCBE	targeted ultraviolet chemical, biological, and explosives

U

U of A	University of Alaska
UARC	University-Affiliated Research Center
UAS	Unmanned Aerial System
UAV	unmanned aviation vehicles
UC	University of California
UCLA	University of California, Los Angeles
UCSB	University of California, Santa Barbara
UE	upper extremity
UGV	unmanned ground vehicle
UH	University of Hawaii
UHRDARM	Ultra-High Resolution Display for Army Medicine
UPMC	University Of Pittsburgh Medical Center
USABCTCoE	US Army Basic Combat Training Center of Excellence
USACHPPM	US Army Center for Health Promotion and Preventive Medicine
USAF	US Air Force
USAID	US Agency for International Development
USAISR	US Army Institute of Surgical Research
USAMMA	US Army Medical Materiel Agency

USAMRIID	US Army Medical Research Institute of Infectious Diseases
USAMRMC	US Army Medical Research and Materiel Command
USAMRU-K	US Army Medical Research Unit - Kenya
USARIEM	US Army Research Institute of Environmental Medicine
USC	University of South Carolina
USGHN	Guam Naval Hospital
USMA	United States Military Academy
USSOCOM	US Special Ops Command
USUHS	Uniformed Services University of Health Sciences
UVBASD	UV Biochemical Agent Surface Detector

V

VA	Department of Veterans Affairs
VCE	Vision Center of Excellence
VH	Virtual Human
VHA	Veterans Health Administration
VHN	Virtual Health Network
VISION	Vision Integrating Strategies in Ophthalmology and Neurochemistry
VL	video laryngoscopy
VLER	Virtual Lifetime Electronic Record
VM	virtual machine
VNS	Vagus Nerve Stimulator
VOIP	Voice-over-Internet Protocol
VR	Virtual Reality
VRE	vancomycin-resistant Enterococci

W

WAP	wireless application protocol
WAROPS	Warrior Optimization System
WIN2	Warrior Wellness Integrated Information Network
WISER	Winter Institute for Simulation Education Research
WMC	Windber Medical Center
WPBF	West Point Bionic Foot
WPIC	Wireless Personal Information Carrier
WPSM	Warfighter Physiological Status Monitor
WRAIR	Walter Reed Army Institute of Research
WRAMC	Walter Reed Army Medical Center

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- Lieutenant General Eric Schoomaker
Surgeon General, US Army

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